Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	4067	d adj (amino acid or aspartate) adj oxidase$ or dao or ddo or daao	US-PGPUB; USPAT	ADJ	OFF	2005/01/11 16:02
L2	36	1 near8 inhibit$	US-PGPUB; USPAT	ADJ	OFF	2005/01/11 16:19
L3	5	1 same (schizophrenia or dression or bipolar)	US-PGPUB; USPAT	ADJ	OFF	2005/01/11 16:03

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	4067	d adj (amino acid or aspartate) adj oxidase$ or dao or ddo or daao	US-PGPUB; USPAT	ADJ	OFF	2005/01/11 16:02
L2	36	1 near8 inhibit$	US-PGPUB; USPAT	ADJ	OFF	2005/01/11 16:19
L3	5	1 same (schizophrenia or dression or bipolar)	US-PGPUB; USPAT	ADJ	OFF	2005/01/11 16:03

PGPUB-DOCUMENT-NUMBER: 20050004104

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20050004104 A1

TITLE: Methods for the protection of memory and cognition

PUBLICATION-DATE: January 6, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Cali, Brian M.	Arlington	MA	US	
Chien, Yueh-Tyng	Newton	MA	US	
Currie, Mark G.	Sterling	MA	US	
Talley, John Jeffrey	Somerville	MA	US	
Zimmerman, Craig	Topsfield	MA	US	

APPL-NO: 10/ 859335

DATE FILED: June 1, 2004

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60475204 20030530 US

US-CL-CURRENT: 514/217.09, 514/323 , 514/414 , 514/419

ABSTRACT:

The invention features certain compounds useful in the treatment of memory disorders, i.e., they reduce or delay memory loss or they enhance memory retention. Because certain of the compounds do not substantially inhibit either COX-1 or COX-2 at therapeutically relevant doses, these compounds are far less likely to cause gastrointestinal ulceration than is indomethacin, which is known to inhibit both COX-1 and COX-2. Certain of the compounds inhibit the activity of DAO at therapeutically relevant doses. Among the memory disorders that can be treated are AD, mild cognitive impairment (MCI; a common precursor to AD), and memory loss or cognitive impairment associated with vascular dementias, amnesia, dementia, AIDS dementia, Huntington's Disease, hydrocephalus, depression, Pick's Disease, Creutzfeldt-Jakob Syndrome, electroconvulsive therapy, or Parkinson's Disease.

CLAIM OF PRIORITY

[0001] This application claims priority under 35 USC .sctn. 119(e) to U.S. Patent Application Ser. No. 60/475,204, filed on May 30, 2003, the entire contents of which is hereby incorporated by reference.

---------- KWIC ---------

Abstract Paragraph - ABTX (1):

The invention features certain compounds useful in the treatment of memory disorders, i.e., they reduce or delay memory loss or they enhance memory retention. Because certain of the compounds do not substantially inhibit either COX-1 or COX-2 at therapeutically relevant doses, these compounds are far less likely to cause gastrointestinal ulceration than is indomethacin,

which is known to inhibit both COX-1 and COX-2. Certain of the compounds inhibit the activity of DAO at therapeutically relevant doses. Among the memory disorders that can be treated are AD, mild cognitive impairment (MCI; a common precursor to AD), and memory loss or cognitive impairment associated with vascular dementias, amnesia, dementia, AIDS dementia, Huntington's Disease, hydrocephalus, depression, Pick's Disease, Creutzfeldt-Jakob Syndrome, electroconvulsive therapy, or Parkinson's Disease.

Summary of Invention Paragraph - BSTX (9):
[0008] It has been suggested that certain inhibitors of D-amino oxidase (DAO), including certain heterocylc-2-carboxylic acids, might be useful for improving memory, learning and cognition in patients suffering from neurodegenerative disorders (U.S. Patent Application Publication U.S. 2003/0162825 A1). Indomethacin has also been shown to be an inhibitor of DAO (Chen et. al 1994 Drug Metabol Drug Interact. 11:153-60). DAO degrades D-serine and other D-amino acids. D-glutamate and D-serine are thought to be agonists of N-methyl-D-aspartate (NMDA)-glutamate receptors that mediate a wide variety of brain activities, including the synaptic plasticity that is associated with certain types of memory and learning (U.S. Pat. No. 20030162825 A1). Thus, it is thought that inhibition of DAO will lead to increased D-serine levels and improved cognitive function.

Summary of Invention Paragraph - BSTX (11):
[0009] The invention features certain compounds useful in the treatment of memory disorders, i.e., they reduce or delay memory loss or they enhance memory retention. Because certain of the compounds do not substantially inhibit either COX-1 or COX-2 at therapeutically relevant doses, these compounds are far less likely to cause gastrointestinal ulceration than is indomethacin, which is known to inhibit both COX-1 and COX-2. Certain of the compounds inhibit the activity of DAO at therapeutically relevant doses. Among the memory disorders that can be treated are AD, mild cognitive impairment (MCI; a common precursor to AD), and memory loss or cognitive impairment associated with vascular dementias, amnesia, dementia, AIDS dementia, Huntington's Disease, hydrocephalus, depression, Pick's Disease, Creutzfeldt-Jakob Syndrome, electroconvulsive therapy, or Parkinson's Disease.

Summary of Invention Paragraph - BSTX (150):
[0148] Also within the invention are compounds having formula II that inhibit the activity of D-aspartate oxidase (DDO), an enzyme that oxidizes D-Asp, D-Glu, D-Asn, D-Gln, D-Asp-dimethyl-ester and N-methyl-D-Asp.

Summary of Invention Paragraph - BSTX (151):
[0149] The compound of the invention can be administered in combination with a DAO or DDO inhibitor or antagonists such as those described in U.S. Application 20030166554, hereby incorporated by reference. Suitable DDO inhibitors can include: aminoethylcysteine-ketimine (AECK, thialysine ketimine, 2H-1,4-thiazine-5,6-dihydro-3-carboxylic acid, S-aminoethyl-L-cysteine ketimine, 2H-1,4-Thiazine-3-carboxylic acid, 5,6-dihydro-); aminoethylcysteine (thialysine); cysteamine; pantetheine; cystathionine; and S-adenosylmethionine.

Detail Description Paragraph - DETX (37):
[0211] Identification of Compounds with DAO Inhibitory Activity

Detail Description Paragraph - DETX (38):
[0212] Porcine kidney D-amino acid oxidase and D-serine can be used to test the DAO inhibitory activity of compounds of the invention. The breakdown of D-serine by DAO produces hydrogen peroxidase, which can be measured using, for example, the Amplex.RTM.t Red Hydrogen Peroxide Assay Kit (Molecular Probes, Inc.; Eugene, Oreg.). Briefly, a working solution is prepared by mixing:

sodium phosphate buffer (8.7 ml, 0.025M, pH 7.4), D-serine solution (1.0 ml, 100 mM in water), horseradish peroxidase (0.2 ml, 200 U/ml in buffer), and Amplex.RTM. Red solution (0.1 ml, 1 mg dye in 200 .mu.l in DMSO (50 .mu.M in DMSO)). A working enzyme solution is prepared by diluting a D-amino oxidase stock solution (65 U/ml) one hundred fold. The working solution (100 .mu.l) is transferred to wells of microtiter plate and a solution of test compound is added. Next, 5 .mu.l of the enzyme solution is added and the rate of hydrogen peroxide release is determined by measuring the oxidation of Amplex.RTM. Red by spectrophotometry (excitation wavelength 544 nm, emission wavelength, 590 nm) after a reaction time of five minutes.

PGPUB-DOCUMENT-NUMBER: 20040229908

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040229908 A1

TITLE: Compositions and methods for the treatment of Parkinson's disease and tardive dyskinesias

PUBLICATION-DATE: November 18, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Nelson, Jodi	Denver	CO	US	

APPL-NO: 10/ 616692

DATE FILED: July 9, 2003

RELATED-US-APPL-DATA:

child 10616692 A1 20030709

parent continuation-in-part-of 10192414 20020709 US PENDING

child 10192414 20020709 US

parent continuation-in-part-of 09615639 20000713 US GRANTED

parent-patent 6417177 US

non-provisional-of-provisional 60143767 19990713 US

non-provisional-of-provisional 60175051 20000107 US

non-provisional-of-provisional 60202140 20000505 US

non-provisional-of-provisional 60479748 20030619 US

US-CL-CURRENT: 514/313

ABSTRACT:

This invention provides compositions and methods for increasing cellular respiration of melanized catecholamine neurons, and methods for alleviating symptoms or stopping appearance and/or progression of symptoms of Parkinson's disease and related conditions, characterized by nigrostriatal degeneration, as well as drug-induced dyskinesias, tardive dyskinesia, Neuroleptic Malignant Syndrome, and negative symptoms of schizophrenia. An effective amount of a neuromelanin-binding composition having a quinoline ring in a suitable pharmaceutical carrier is administered to patient in need of such treatment. Preferably the composition comprises (-)-chloroquine diphosphate. Selected adjuvants are also provided as part of the compositions of this invention.

[0001] This application is a continuation-in-part of U.S. patent application Ser. No. 10/192,414 filed Jul. 9, 2002, which is a continuation-in part of

U.S. patent application Ser. No. 09/615,639 filed Jul. 13, 2000, now U.S. Pat. No. 6,417,177 issued Jul. 9, 2002, which takes priority from U.S. Patent Application No. 60/143,767 filed Jul. 13, 1999, U.S. Patent Application No. 60/175,051 filed Jan. 7, 2000, and U.S. Patent Application No. 60/202,140 filed May 5, 2000. This application also takes priority from U.S. Provisional Patent Application Ser. No. 60/479,748 filed Jun. 19, 2003. All of the foregoing applications are incorporated herein by reference to the extent not inconsistent herewith.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (135):

[0134] Enhancing agents are agents, which act to increase levels of active ingredient in the brain or to increase dopamine levels in the brain. Preferred enhancing agents are histamine (H.sub.1) receptor antagonists. These act to counteract increased histamine bioavailability resulting from active ingredient, especially CQ, inhibition of histamine methyltransferase (HMT) and diamine oxidase (DAO, the two primary degradative histamine pathways by chloroquine, and to minimize histamine-associated adverse events, which have been observed with antimalarial treatment formulas.

PGPUB-DOCUMENT-NUMBER: 20040229241

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040229241 A1

TITLE: Cloned mammalian polyamine oxidase

PUBLICATION-DATE: November 18, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Casero, Robert A.	Glenn Aron	MD	US	
Wang, Yanlin	Baltimore	MD	US	

APPL-NO: 10/ 733020

DATE FILED: December 12, 2003

RELATED-US-APPL-DATA:

child 10733020 A1 20031212

parent continuation-in-part-of PCT/US02/18666 20020613 US PENDING

non-provisional-of-provisional 60297815 20010613 US

US-CL-CURRENT: 435/6, 435/191 , 435/320.1 , 435/325 , 435/69.1 , 536/23.2

ABSTRACT:

Polynucleotides and the corresponding polypeptides of cloned mammalian polyamine oxidase (PAO) (including various isoforms and truncated forms) are provided. Also provided are antibodies to cloned mammalian PAO, and vectors and host cells containing cloned PAO, and methods for their use.

---------- KWIC ---------

Detail Description Paragraph - DETX (126):

[0152] Total cellular RNA was extracted from the lung cancer cell lines using Trizol reagent (Invitrogen) according to the manufacturer's protocol. For Northern blotting, total RNA (20 lg) was separated on a denaturing 1.5% agarose gel containing 6% formaldehyde and transferred to Zetaprobe membrane (Bio-Rad). Random primer-labeled PAOh1 cDNA was used as probe to estimate PAOh1/SMO expression [42]. Blots were stripped and reprobed with an 18S ribosomal cDNA to provide a loading control. Analysis of polyamine content, SSAT and PAOh1/SMO activity. Intracellular polyamine concentrations were determined using the precolumn dansylation labeling, reverse-phase high-pressure liquid chromatography method as described by Kabra et al. [22] using 1,7-diaminoheptane as an internal standard. Polyamine concentrations are reported as nanomoles per milligram protein for each sample, where lysate protein content was measured by the method of Bradford [5]. SSAT activity of cellular extracts was measured as previously described [8]. The PAOh1/SMO enzyme activity in the cell lysates was assayed as previously described [42] by the method of Suzuki et al. [38] using 250 .mu.M spermine as the substrate. The PAOh1/SMO assays were performed in the presence of 1.0 mM pargyline and 0.1 mM semicarbizide as inhibitors of monoamine oxidase (MAO) and diamine oxidase

(DAO), respectively.

Detail Description Paragraph - DETX (135):

[0161] To determine the basic structural requirements of PAOh1/SMO induction in NCI A549 cells, the ability of eight polyamine analogues that are undergoing or are being considered for clinical trials were examined for their ability to induce PAOh1/SMO activity. The symmetrically substituted BENSpm, and the asymmetrically substituted CPENSpm, CHENSpm, and IPENSpm led to significant induction of PAOh1/SMO after 24 h exposure to 10 .mu.M of each analogue (FIG. 31). The oligoamine analogues, SLIL 11144, 11150, 11158, and the conformationally restricted analogue, SLIL 11093, did not induce PAOh1/SMO. The results of these studies suggest that one structural requirement for PAOh1/SMO induction is the presence of multiple aminopropyl moieties within the analogue structure. It is also important to note that the polyamine oxidase inhibitor MDL 72,527 significantly inhibited the PAOh1/SMO activity induced by the analogues, but did not significantly reduce the basal levels of oxidase activity. These data are consistent with the possibility that there is a basal oxidase activity in the NCI A549 cells that is not inducible by polyamine analogues and is not inhibited by PAOh1/SMO, MAO, or DAO inhibitors.

PGPUB-DOCUMENT-NUMBER: 20040157926

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040157926 A1

TITLE: Pharmaceutical compositions for the treatment of movement disorders

PUBLICATION-DATE: August 12, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Heresco-Levy, Uriel	Jerusalem	NY	IL	
Javitt, Daniel C.	Bardonia		US	

APPL-NO: 10/ 744452

DATE FILED: December 23, 2003

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
IL	154,318	2003IL-154,318	February 6, 2003

US-CL-CURRENT: 514/561

ABSTRACT:

The invention provides a pharmaceutical composition, medical food, dietary supplement or micronutrient for the treatment of a movement disorder comprising an NMDAR agonist or partial agonist as active ingredient therein in combination with a pharmaceutically acceptable carrier.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (2):

[0002] NMDAR are a type of receptor for the excitatory neurotransmitter glutamate. MDAR contain additional modulatory sites, including the following: glycine binding site, polyamine binding site, redox site, Zinc (Zn) site, phosphorylation sites, post-synaptic membrane docking sites and protein-protein interaction sites (e.g., Lynch and Guttman, 2001). The glycine binding site is sensitive to monocarboxyllic amino acids including the endogenous amino acids glycineD-serine and D-alanine. Glycine is synthesized via serine or threonine by serine hydroxymethyltransferase. Synaptic glycine concentrations are regulated by type 1 (GLYT1) and type 2 (GLYT2) glycine transporters, as well as by other amino acid transporters belonging to Systems A, L, ASC, and N (Sershen et al., 1979). GLYT1 transport inhibitors, such as N[3-(4'-fluorophenyl)-3-(4'-phenylphenoxy)propyl]sarcosine (NFPS), potentiate NMDAR activity in vivo, (Bergeron et al., 1989; Klitenick et al., 2001) suggesting a critical role for glycine transporters in NMDAR regulation. Methylated glycine derivates (e.g., methylglycine, sarcosine) may serve as non-specific glycine transport inhibitors D-serine and D-alanine are metabolized by D-amino acid oxidase (DAAO), which is localized particularly in hindbrain. Further, DAAO is regulated by a novel protein termed G72, which may affect metabolic activity of the DAAO enzyme (Chumakov et al., 2002). Glycine, D-serine and D-alanine levels in brain may be modulated by administering exogenous compound (i.e., glycine, D-serine or D-alanine), or naturally occurring precursors to these

compounds including but not limited to L-serine, L-phosphoserine, D-phosphoserine and threonine, or by modulation of the synthetic enzymes serine hydroxymethyltransferase or serine racemase. D-Serine or D-alanine levels may also be increased by modulation inhibiting D-serine or D-alanine breakdown, for example, by antagonizing DAAO activity either directly or indirectly (e.g., via modulatory proteins).

Detail Description Paragraph - DETX (33):

[0043] The examples above demonstrate effectiveness of two full NMDAR agonists, as well as a partial NMDAR agonist in treatment of antipsychotic-induced movement disorder, including Parkinsonian and dyskinetic symptoms. Other methods for augmenting NMDA transmission via the glycine binding site have been proposed including use of glycine transport inhibitors (aka transport antagonists, uptake inhibitors, uptake antagonists), acting at the GLYT1, GLYT2, System A, System ASC or other glycine transport sites, and modulators of D-serine metabolism including inhibitor of b-serine transport and of D-amino acid oxidase. Agents may be screened for effectiveness in stimulating NMDA transmission in vitro using assays, for example, measuring modulation of NMDAR-mediatedactivity in hippocampal slices (Bergeron et al., 1998) or of NMDAR-stimulated dopamine release in isolated mouse striatum (Javitt et al., 2000). Agents may be screened in vivo using assays, for example, measuring amphetamine induced dopamine release or NMDAR-mediated electrophysiological activity (Klitenick et al., 2001). Agents will be effective in ameliorating movement disorders at doses sufficient to potentiate NMDAR-mediated neurotransmission in vivo.

Claims Text - CLTX (18):

17. The method of claim 6 in which D amino acid oxidase inhibitors are used in place of glycine-site agonists at doses sufficient to augment NMDAR-mediated neurotransmission.

PGPUB-DOCUMENT-NUMBER: 20040072771

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040072771 A1

TITLE: Methods for genetic modification of hematopoietic progenitor cells and uses of the modified cells

PUBLICATION-DATE: April 15, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
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Sun, Lun -Quan	Eastwood		AU	
MacPherson, Janet L.	Leichhardt		AU	
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APPL-NO: 10/ 192980

DATE FILED: July 10, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60304127 20010710 US

non-provisional-of-provisional 60304283 20010710 US

non-provisional-of-provisional 60343484 20011221 US

non-provisional-of-provisional 60386063 20020604 US

US-CL-CURRENT: 514/44, 424/93.21

ABSTRACT:

Described are compositions and methods relating to gene therapy, particularly as applied to hematopoietic progenitor (HP) cells, to transduced cells and methods of obtaining them, and to methods of using them to provide prolonged engraftment of modified hematopoietic cells in human subjects. The invention particularly relates to ex vivo gene therapy of HP cells for treatment or prevention of HIV infection.

[0001] This application claims benefit of U.S. Provisional Application No. 60/304,127, filed Jul. 10, 2001, U.S. Provisional Application No. 60/304,283, Jul. 10, 2001, U.S. Provisional Application No. 60/343,484, filed Dec. 21, 2001, and U.S. Provisional Application No. 60/386,063, filed Jun. 4, 2002, the contents of all of which are hereby incorporated by reference.

---------- KWIC ---------

Detail Description Paragraph - DETX (149):
[0201] Efficient transduction of human HP cells with murine oncoretroviral

vectors (for example, those based on MMLV) and some other retroviral vectors requires induction of cell cycle, for example with one or more cytokines (growth factors) (Dao and Nolta 1999) or inhibitors of cell cycle control. The combination of thrombopoietin (TPO), Flt-3 ligand (FL) and Kit ligand (K L, also known as SCF) has been used in vitro (Murray et al 1999, Ng et al 2002). The combination of MGDF, SCF and FL was used in repopulation assays in primates (Wu et al 2000). Amado et al showed that treatment of cells with MGDF and SCF better supported the survival of thymocyte precursor cells than other combinations of factors in a mouse model (Amado et al 1998). IL-3, IL-6, SCF or TPO or combinations thereof have been shown to have beneficial effects on HP cell transduction (Nolta et al 1992, Hennemann et al 1999). The combinations FL/SCF/IL-3/IL-6, SCF/G-CSF, FL/SCF/TPO/IL-6, FL/SCF/G-CSF, FL/SCF/TPO, and FL/SCF/GM-CSF have also been used in large animal models (Richter and Karlson 2001). There is evidence, however, that the combination of IL-3, IL-6 and SCF may impair engraftment (Peters et al 1996). Other approaches to induce cycling of HP cells include the use of inhibitors (eg antisense molecules or antibodies) of p27 (kip1) (Dao et al 1998, Cheng et al 2000) or transforming growth factor beta-1 (Ducos et al 2000, Imbert et al 1998) to increase cell numbers. However, the ability of cells stimulated in any of these ways and then transduced to confer long term engraftment in humans was unknown prior to this invention.

PGPUB-DOCUMENT-NUMBER: 20040053989

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040053989 A1

TITLE: Dithiolthione compounds for the treatment of neurological disorders and for memory enhancement

PUBLICATION-DATE: March 18, 2004

INVENTOR-INFORMATION:

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Armstrong, Paul	Belfast		GB	

APPL-NO: 10/ 612476

DATE FILED: July 2, 2003

RELATED-US-APPL-DATA:

child 10612476 A1 20030702

parent continuation-of 09627641 20000728 US ABANDONED

non-provisional-of-provisional 60145964 19990729 US

non-provisional-of-provisional 60198338 20000418 US

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
IE	2000/0302	2000IE-2000/0302	April 13, 2000
IE	2000/0304	2000IE-2000/0304	April 13, 2000

US-CL-CURRENT: 514/440, 514/210.19 , 514/217.03 , 514/326 , 514/422

ABSTRACT:

The invention provides methods to treat neurological disorders such as Alzheimer's disease, or to slow the progression of such diseases, or to treat and/or prevent other disorders as disclosed in the specification, by administering to patients, or delivering to the tissues of such patients, oltipraz or related compounds as disclosed in the specification.

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to the following copending applications: U.S. provisional application No.60/145,964 filed Jul. 29, 1999; U.S. provisional application No.60/198,338 filed Apr. 18, 2000; Irish patent application no.2000/0302 filed Apr. 13, 2000; and Irish patent application no. 2000/10303 filed Apr. 13, 2000; all of which are incorporated herein by reference.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (3):

[0003] This invention relates to methods of treating subjects who have, or who are at risk of having, a faulty memory, a degenerative disorder, a neurodegenerative disorder, a neurodegenerative-related disorder, or a parasite infection such as malaria, sleeping sickness or a trypanosome infection, using dithiolthione compounds or inhibitors of D-amino acid oxidase. This invention also relates to improved methods of making 1,2-dithiole-3-thiones, including oltipraz (CAS Number 6422-421-1). This invention also relates to a diagnostic assay for neurodegenerative disorders.

Summary of Invention Paragraph - BSTX (10):
[0010] WO9827970 (Fiander et al) discloses the use of Michael reaction acceptors, for use in protecting cells against the toxic effects of oxygen containing free radicals in mammals. WO9827970 does not teach the use of compounds that inhibit DAAO, chelate iron and/or copper or enhance phase II detoxification enzymes in prophylaxis and treatment of degenerative disorders including Alzheimer's disease.

Summary of Invention Paragraph - BSTX (50):
[0048] Although the instant invention is not bound by any theory, it is believed that with aging, the D-amino acid percentage in a subject increases so that a larger percentage of amino acids present in the cell will be D-amino acids. The proteins thus formed will then be made up of a percentage of D-amino acids and will not function. The body produces D-amino acid oxidase (DAAO) to metabolize them, producing ammonia and hydrogen peroxide, which are toxic to cells. In young cells, the phase II detoxification enzymes, e.g., glutathione reductase, are present in sufficient quantity to combat hydrogen peroxide production, but their levels are thought to reduce with aging. The compounds of the instant invention, particularly oltipraz, are believed to inhibit DAAO and thus enhance the effect of glutathione reductase enzymes. Other explanations are possible and are mentioned herein.

Summary of Invention Paragraph - BSTX (91):
[0089] In one embodiment, the compounds of the present invention are D-amino acid oxidase inhibitors. By inhibiting D-amino acid oxidase, the production of highly toxic substances i.e. NH.sub.3 and H.sub.2O.sub.2, is greatly reduced. These substances are greatly involved in lipid peroxidation, possibly caused by free radical formation, and perhaps is one of the causative factors of neuronal death.

Summary of Invention Paragraph - BSTX (212):
[0210] The present invention also provides a method for treating degenerative and related disorders comprising administering a pharmaceutical formulation containing one or more D-amino acid oxidase inhibitors.

Summary of Invention Paragraph - BSTX (214):
[0212] The present invention also provides a method for prophylactically and therapeutically treating degenerative and related disorders comprising administering to mammals a pharmaceutical formulation containing one or more inhibitors of the enzyme D-amino acid oxidase

Summary of Invention Paragraph - BSTX (227):
[0225] The invention provides for the use of the compunds disclosed herein, e.g., the dithiolthione compounds such as oltipraz, ADT or ADO, to inhibit the activity of the DAAO enzyme in vitro or in vivo.

Summary of Invention Paragraph - BSTX (255):
[0253] The compounds disclosed herein are thus useful for the prevention or treatment of the symptoms of neurodegenerative disorders such as AD, or for treating or slowing progression of malaria or a trypanosome infection, or they

are useful for enhancing the long term or short term memory in a subject in need thereof. The compounds are also useful for treating long term or short term memory loss associated with neurodegenerative disorders or related degenerative conditions, and for slowing the progression or rate of memory loss and for reducing the level of iron in the cells of a living subject, for inhibiting D-amino acid oxidase in a subject, and for enhancing a phase II detoxification enzyme in a subject, preferably selected from GST, .gamma.-GCS, glutathione reductase, glutathione peroxidase, epoxide hydrase, AFB.sub.1 aldehyde reductase, glucuronyl reductase, glucose-6-phosphate dehydrogenase, UDP-glucuronyl transferase and AND(P)H:quinone oxidoreductase.

Summary of Invention Paragraph - BSTX (258):
[0256] 2. The method of embodiment 1 wherein the compounds of the present invention are D-amino acid oxidase inhibitors.

Summary of Invention Paragraph - BSTX (401):
[0399] 104. The method of embodiment 103 wherein, the compounds of the present invention are D-amino acid oxidase inhibitors.

Summary of Invention Paragraph - BSTX (556):
[0554] 213. Use of an effective amount of a D-amino acid oxidase inhibitor to treat or prevent a neurodegenerative disorder or a neurodegenerative-related disorder comprising administering to a mammal in need thereof an effective amount of the D-amino acid oxidase inhibitor.

Summary of Invention Paragraph - BSTX (557):
[0555] 214. Use of embodiment 213 wherein the D-amino acid oxidase inhibitor is a compound of the invention, e.g., a compound of FIG. 1-FIG. 4, oltipraz or a compound described in any of the foregoing numbered embodiments, a composition described in any of the following numbered embodiments.

Claims Text - CLTX (9):
8. The method of claim 1 wherein said compound is a D-amino acid oxidase inhibitor and cellular degeneration is slowed or arrested.

Claims Text - CLTX (18):
17. The method of claim 11 wherein said compound is a D-amino acid oxidase inhibitor and cellular degeneration is slowed or arrested.

Claims Text - CLTX (28):
27. The method of claim 20 wherein said compound is a D-amino acid oxidase inhibitor and cellular degeneration is slowed or arrested.

Claims Text - CLTX (39):
38. The method of claim 30 wherein said compound is a D-amino acid oxidase inhibitor.

Claims Text - CLTX (65):
64. Use of a D-amino acid oxidase inhibitor to treat or prevent a degenerative disorder, a neurodegenerative disorder, a degenerative-related disorder, a neurodegenerative-reiated disorder, comprising administering to a mammal in need thereof an effective amount of the D-amino acid oxidase inhibitor.

PGPUB-DOCUMENT-NUMBER: 20040033972

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040033972 A1

TITLE: Treatment of mycobacterium tuberculosis with antisense polynucleotides

PUBLICATION-DATE: February 19, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
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APPL-NO: 10/ 168244

DATE FILED: August 29, 2002

PCT-DATA:
APPL-NO: PCT/US00/34688
DATE-FILED: Dec 20, 2000
PUB-NO:
PUB-DATE:
371-DATE:
102(E)-DATE:

US-CL-CURRENT: 514/44, 514/15 , 514/252.13 , 514/291 , 514/354 , 536/23.2

ABSTRACT:

Methods of inhibiting the proliferation of Mycobacterium tuberculosis comprising contacting Mycobacterium tuberculosis with an effective amount of a polynucleotide complementary to an mRNA transcript expressed by Mycobacterium tuberculosis are provided. Typical methods of the invention utilize phosphorothioate modified antisense polynucleotides (PS-ODNs) against the mRNA of M.tuberculosis genes such as glutamine synthetase, aroA,ask, groES, and the genes of the Antigen 85 complex.

[0001] This application claims the benefit of U.S. provisional patent application No. 60/171,929, filed Dec. 22, 1999, the entire contents of which are incorporated herein by reference.

---------- KWIC --------

Brief Description of Drawings Paragraph - DRTX (15):

[0028] FIG. 14 shows the inhibition of cell proliferation of M. smegmatis 1-2c.+-.rM.tb. GS broth cultures by modified antisense PS-ODN 269-275 at 10 .mu.M. This Figure shows that 269-275-DAO does not inhibit M. smegmatis.

Detail Description Paragraph - DETX (170):

[0187] 2. 269-275-DAO did not inhibit M. smegmatis, as expected.

Detail Description Paragraph - DETX (172):
[0189] FIG. 13 shows that 269-275-DAO was mote effective at 10.mu.M than PS-ODN 269-275 at inhibiting the growth of M. tuberculosis. The control ODN yielded no inhibition of growth, i.e. it was equivalent to no ODN being added.

Detail Description Paragraph - DETX (173):
[0190] FIG. 14 shows that 269-275-DAO does not inhibit M. smegmatis.

PGPUB-DOCUMENT-NUMBER: 20030185754

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030185754 A1

TITLE: Treatment of CNS disorders using D-amino acid oxidase and D-aspartate oxidase antagonists

PUBLICATION-DATE: October 2, 2003

US-CL-CURRENT: 424/9.2, 800/3

APPL-NO: 10/ 051681

DATE FILED: January 16, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60261883 20010116 US

non-provisional-of-provisional 60305445 20010713 US

non-provisional-of-provisional 60333881 20011119 US

RELATED APPLICATIONS

[0001] This application claims priority from U.S. Provisional Patent Application Serial Nos. 60/261,883, filed Jan. 16, 2001; 60/305,445, filed Jul. 13, 2001; 60/___,___, filed Oct. 22, 2001; and 60/333,881 filed Nov. 19, 2001, which disclosures are hereby incorporated by reference in their entireties.

PGPUB-DOCUMENT-NUMBER: 20030166554

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030166554 A1

TITLE: Treatment of CNS disorders using D-amino acid oxidase and D-aspartate oxidase antagonists

PUBLICATION-DATE: September 4, 2003

US-CL-CURRENT: 514/12, 424/9.2 , 514/227.5 , 514/231.5 , 514/253.01 , 514/340 , 514/357 , 514/89 , 800/3

APPL-NO: 10/ 211160

DATE FILED: August 1, 2002

RELATED-US-APPL-DATA:

child 10211160 A1 20020801

parent continuation-in-part-of 10051681 20020116 US PENDING

non-provisional-of-provisional 60261883 20010116 US

non-provisional-of-provisional 60305445 20010713 US

non-provisional-of-provisional 60345211 20011022 US

non-provisional-of-provisional 60333881 20011119 US

RELATED APPLICATIONS

[0001] This application is a continuation-in-part of U.S. Ser. No. 10/051,681 claims priority from U.S. Provisional Patent Application Serial Nos. 60/261,883, filed Jan. 16, 2001; 60/305,445, filed Jul. 13, 2001; 60/345,211, filed Oct. 22, 2001; and 60/333,881 filed Nov. 19, 2001, which disclosures are hereby incorporated by reference in their entireties.

PGPUB-DOCUMENT-NUMBER: 20030162825

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030162825 A1

TITLE: D-amino acid oxidase inhibitors for learning and memory

PUBLICATION-DATE: August 28, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Heefner, Donald L.	Hudson	MA	US	
Currie, Mark G.	Sterling	MA	US	
Rossi, Richard Filip JR.	Norton	MA	US	
Zepp, Charles M.	Hardwick	MA	US	

APPL-NO: 10/ 292368

DATE FILED: November 12, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60332343 20011109 US

US-CL-CURRENT: 514/419, 514/290 , 514/423 , 514/461

ABSTRACT:

Methods and pharmaceutical compositions which inhibit the activity of D-amino acid oxidase (DAO) are disclosed. Inhibition of DAO improves memory, learning and cognition in individuals suffering from neurodegenerative diseases such as Alzheimer's, Huntington's or Parkinson's diseases; the methods and pharmaceutical compositions which inhibit the activity of DAO also improve cognitive dysfunctions associated with aging and improve catatonic schizophrenia. Several genera of heterocycle-2-carboxylic acids are disclosed as DAO inhibitors.

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority from U.S. provisional application, serial No. 60/332,343, filed Nov. 9, 2001, the entire disclosure of which is incorporated herein by reference.

---------- KWIC ---------

Abstract Paragraph - ABTX (1):

Methods and pharmaceutical compositions which inhibit the activity of D-amino acid oxidase (DAO) are disclosed. Inhibition of DAO improves memory, learning and cognition in individuals suffering from neurodegenerative diseases such as Alzheimer's, Huntington's or Parkinson's diseases; the methods and pharmaceutical compositions which inhibit the activity of DAO also improve cognitive dysfunctions associated with aging and improve catatonic schizophrenia. Several genera of heterocycle-2-carboxylic acids are disclosed as DAO inhibitors.

Title - TTL (1):

D-amino acid oxidase inhibitors for learning and memory

Summary of Invention Paragraph - BSTX (19):
[0017] In one aspect, the invention relates to a method for improving learning and memory comprising administering a D-amino acid oxidase inhibitor. D-amino acid oxidase inhibitors whose activities are demonstrated below include compounds of formula: 2

Summary of Invention Paragraph - BSTX (25):
[0023] In a second aspect the invention relates to methods for treating a condition chosen from epilepsy, neurotoxic injury, dementia, schizophrenia and neurodegenerative disease comprising administering a therapeutically effective amount of a D-amino acid oxidase (DAO) inhibitor.

Detail Description Paragraph - DETX (2):
[0030] The invention derives from a discovery that neurodegenerative disorders and deficits in learning and memory can be alleviated by administration of D-amino acid oxidase (DAO) inhibitors. N-methyl-D-aspartate (NMDA)-glutamate receptors are expressed at excitatory synapses throughout the central nervous system (CNS). These receptors mediate a wide range of brain processes, including synaptic plasticity associated with certain forms of memory formation and learning. NMDA-glutamate receptors require binding of two agonists to effect neurotransmission. One of these agonists is the excitatory amino acid L-glutamate, while the second agonist, at the so-called "strychnine-insensitive glycine site", is now thought to be D-serine. In animals, D-serine is synthesized from L-serine by serine racemase and degraded to its corresponding ketoacid by DAO. Together, serine racemase and DAO are thought to play a crucial role in modulating NMDA neurotransmission by regulating CNS concentrations of D-serine.

Detail Description Paragraph - DETX (3):
[0031] The present invention relates to methods and pharmaceutical compositions which inhibit the activity of DAO, thereby improving memory, learning and cognition in individuals suffering from neurodegenerative diseases such as Alzheimer's, Huntington's or Parkinson's diseases; the methods and pharmaceutical compositions which inhibit the activity of DAO also improve cognitive dysfunctions associated with aging and improve catatonic schizophrenia. DAO inhibitors can also be used in conjunction with therapy involving administration of D-serine or an analog thereof, such as a salt of D-serine, an ester of D-serine, alkylated D-serine, or a precursor of D-serine, or can be used in conjunction with therapy involving administration of antipsychotics, antidepressants, psychostimulants, and/or Alzheimer's disease therapeutics. Examples of disorders that can be treated by the methods of the invention include schizophrenia, autism, depression, benign forgetfulness, childhood learning disorders, close head injury, and attention deficit disorder.

Detail Description Paragraph - DETX (25):
[0053] The invention offers several advantages over many art-known methods for treating neuropsychiatric disorders. For example, unlike many conventional antipsychotic therapeutics, DAO inhibitors can produce a desirable reduction in the cognitive symptoms of schizophrenia. Conventional antipsychotics often lead to tardive dyskinesia (irreversible involuntary movement disorder), extra pyramidal symptoms, and akathesia.

Detail Description Paragraph - DETX (26):
[0054] For the purposes of the invention, a D-amino acid oxidase inhibitor is defined as a compound that exhibits an IC.sub.50 less than 100 .mu.M against porcine kidney D-amino acid oxidase in the test described herein, in Example 1.

Detail Description Paragraph - DETX (27):
[0055] D-amino acid oxidase inhibitors include compounds of formula 4

Detail Description Paragraph - DETX (33):
[0061] Preferred D-amino acid oxidase inhibitors include: 5

Detail Description Paragraph - DETX (34):
[0062] A particularly preferred D-amino acid oxidase inhibitor is 2-indole carboxylic acid.

Detail Description Paragraph - DETX (35):
[0063] Other preferred D-amino acid oxidase inhibitors include compounds of formula II: 6

Detail Description Paragraph - DETX (42):
[0070] In a second aspect the invention relates to methods for treating a condition chosen from epilepsy, neurotoxic injury, dementia, schizophrenia and neurodegenerative disease comprising administering a therapeutically effective amount of a D-amino acid oxidase (DAO) inhibitor. Neurodegenerative diseases may include Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, Down syndrome, neuropathic pain, dementia, stroke, mental retardation, ADHD and schizophrenia. Both the first aspect of the invention (learning and memory) and this second aspect envision the use of any and all D-amino acid oxidase (DAO) inhibitors in the method of treatment. However, due to the peculiarities of patent law, and having nothing whatever to do with the scope of the inventors' conception of the invention, certain DAO inhibitors appear from a preliminary search of the literature ineligible to be claimed for the second utility. Thus, for example, indole-2-carboxylic acid, 5-chloroindole-2-carboxylic acid, 5-methoxyindole-2-carboxylic acid and compounds of the generic formula 8

Detail Description Paragraph - DETX (43):
[0071] while they are part of the inventive concept, have been excluded from the claims to treating epilepsy, neurotoxic injury, dementia, schizophrenia and neurodegenerative disease. Excluded genera are those wherein m is 1 to 4; R.sup.3a is hydrogen or methyl; R.sup.5a, R.sup.6a, R.sup.7a and R.sup.8a are chosen from hydrogen and halogen; and R.sup.11 is chosen from hydroxy, lower alkoxy, di(lower alkyl)amino and sulfonamide. It may be found upon examination that methods employing certain members of the excluded genera are patentable to the inventors in this application or that additional species and genera not presently excluded are not patentable to the inventors in this application. In either case, the exclusion of species and genera in applicants' claims are to be considered artifacts of patent prosecution and not reflective of the inventors' concept or description of their invention, which encompasses all DAO inhibitors.

Detail Description Paragraph - DETX (44):
[0072] In a particular embodiment, DAO inhibitors for treating epilepsy, neurotoxic injury, dementia, schizophrenia, if neurodegenerative disease are compounds of formula 9

Detail Description Paragraph - DETX (51):
[0079] If desired, a pharmaceutical composition containing one or more of the subject DAO inhibitors can be administered to a patient suffering from schizophrenia along with, or in sequence with, a drug for treating schizophrenia (e.g., olanzapine, clozapine, haloperidol, and the like). Similarly, the subject DAO inhibitors can be used in combination with, or in sequence with, other antipsychotics (e.g., "typical," "atypical," and depot

antipsychotics for treating schizophrenia and other psychotic conditions), psychostimulants (for treating attention deficit disorder, depression, or learning disorders), or Alzheimer's disease therapeutics (for treating Alzheimer's disease). Such pharmaceutical compositions and methods for conjoint therapies are included within the invention.

Detail Description Paragraph - DETX (52):
[0080] The phrase "therapeutically effective amount" as used herein means that amount of a compound, material, or composition comprising a compound of the present invention which is effective for producing some desired therapeutic effect by inhibition of DAO in at least a sub-population of cells in an animal and thereby blocking the biological consequences of that pathway in the treated cells, at a reasonable benefit/risk ratio applicable to any medical treatment.

Detail Description Paragraph - DETX (60):
[0088] While it may be possible for DAO inhibitors to be administered as the raw chemical, it is preferable to present them as a pharmaceutical composition. According to a further aspect, the present invention provides a pharmaceutical composition comprising a compound of formula I or II or a pharmaceutically acceptable salt or solvate thereof, together with one or more pharmaceutically carriers thereof and optionally one or more other therapeutic ingredients. The carrier(s) must be "acceptable" in the sense of being compatible with the other ingredients of the formulation and not deleterious to the recipient thereof.

Detail Description Paragraph - DETX (78):
Enhancement of Learning and Memory by DAO Inhibitors in Animal Model (Morris Water Maze Test)

Claims Text - CLTX (1):
1. A method for improving learning and memory and cognition, or a combination thereof, comprising administering to a mammal an amount of a D-amino acid oxidase inhibitor sufficient to improve learning and memory.

Claims Text - CLTX (2):
2. A method according to claim 1 wherein said D-amino acid oxidase inhibitor is a compound or a pharmaceutically acceptable salt or solvate of a compound of formula: 22wherein A is --O-- or --NH--; R.sup.1 is hydrogen or lower alkyl; R.sup.2 is hydrogen or lower alkyl; or taken together R.sup.1 and R.sup.2 form a six-membered ring, optionally substituted with one or more substituents chosen from halogen and hydroxyl.

Claims Text - CLTX (3):
3. A method according to claim 1, wherein said D-amino acid oxidase inhibitor is a compound, or a pharmaceutically suitable salt or solvate of a compound of formula: 23wherein R.sup.11 and R.sup.12 are independently hydrogen, alkyl, substituted alkyl, aryl, or alkylaryl; R.sup.13 is hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, alkylaryl or substituted alkylaryl; and R.sup.14, R.sup.15, R.sup.16 and R.sup.17 are independently hydrogen, hydroxy, halo, amino, cyano, nitro, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylakyl, alkoxy.

Claims Text - CLTX (4):
4. A method according to claim 3 wherein said D-amino acid oxidase inhibitor is a compound or a pharmaceutically acceptable salt or solvate of a compound chosen from: 24

Claims Text - CLTX (6):
6. A method according to claim 1 wherein said D-amino acid oxidase inhibitor is a compound or a pharmaceutically acceptable salt or solvate of a

compound of formula: 25wherein R.sup.3 is hydrogen or methyl; R.sup.4 is chosen from alkyl, aryl, substituted alkyl and substituted aryl; R.sup.5, R.sup.6 and R.sup.7 are chosen independently from hydrogen, halogen, nitro, lower alkyl and lower alkoxy; and the dashed line bond represents an optional double bond which may be located in either of the two positions shown.

Claims Text - CLTX (7):

7. A method for treating a condition chosen from epilepsy, neurotoxic injury, dementia, schizophrenia and neurodegenerative disease comprising administering to a patient in need of treatment a therapeutically effective amount of a **D-amino acid oxidase (DAO) inhibitor, with the proviso that said DAO inhibitor** is not indole-2-carboxylic acid, 5-chloroindole-2-carboxylic acid, 5-methoxyindole-2-carboxylic acid or a compound of the generic formula 26wherein m is 1 to 4 R.sup.3a is hydrogen or methyl; R.sup.5a, R.sup.6a, R.sup.7a and R.sup.8a are chosen from hydrogen and halogen; and R.sup.11 is chosen from hydroxy, lower alkoxy, di(lower alkyl)amino and sulfonamide.

Claims Text - CLTX (14):

14. A method for treating a condition chosen from Parkinson's disease, Alzheimer's disease, Huntington's disease, epilepsy, neuropathic pain, dementia, ADHD and schizophrenia comprising administering to a patient in need of treatment a therapeutically effective amount of a **D-amino acid oxidase inhibitor having an IC.sub.50 less than 10 .mu.M against porcine kidney D-amino acid oxidase**.

PGPUB-DOCUMENT-NUMBER: 20030144705

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030144705 A1

TITLE: Methods and apparatus for controlling a pacing system in the presence of EMI

PUBLICATION-DATE: July 31, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Funke, Hermann D.	Gemmenich		BE	

APPL-NO: 10/ 143392

DATE FILED: May 10, 2002

RELATED-US-APPL-DATA:

child 10143392 A1 20020510

parent continuation-in-part-of 10059586 20020129 US PENDING

US-CL-CURRENT: 607/27

ABSTRACT:

Pacing systems are disclosed including detectors for detecting the presence of electromagnetic interference and setting an interference state pacing mode and pacing rate. The interference state pacing mode and pacing rate are altered as a function of patient pacemaker dependency and the prevailing mean heart rate. When pacemaker dependency exists, the pacing rate is maintained and even increased from the prevailing mean heart for the duration of the interference state. When the patient is determined to not be pacemaker dependent, pacing is inhibited or suspended for the duration of the interference state.

CROSS-REFERENCE TO RELATED APPLICATION

[0001] This application is a continuation-in-part of U.S. patent application Ser. No. 10/059,586 filed Jan. 29, 2002 for METHOD AND APPARATUS FOR CONTROLLING AN IMPLANTABLE MEDICAL DEVICE IN RESPONSE TO THE PRESENCE OF A MAGNETIC FIELD AND/OR HIGH FREQUENCY RADIATION INTERFERENCE SIGNALS (P-8110.00) in the name of Hermann D. Funke.

---------- KWIC ---------

Detail Description Paragraph - DETX (51):

[0089] In FIG. 9(b), the A-P % is compared to the fixed or programmable pacemaker dependency thresholds comprising an atrial pacemaker dependency threshold, e.g., 60%, in decision step 930. If the prevailing A-P % is greater than 60% (A-P %>60%), the patient is declared pacemaker dependent in decision step 940. In step 940, the pacing mode is switched from the prevailing DDD(R) pacing mode to the classic DDO(R) pacing mode where atrial and ventricular pacing is not inhibited or triggered by a atrial and ventricular sense events, and the interference state pacing rate is set to

MHR+10 bpm. If the prevailing A-P % is not greater than 60% (A-P %<60%), the patient is declared somewhat pacemaker independent in decision step 935. In step 935, the pacing mode is switched from the prevailing DDD(R) pacing mode to the classic DDO(R) pacing mode, and the interference state pacing rate is set to MHR+20 bpm. The 10 bpm and 20 bpm increments can either be fixed or made programmable. The interference state pacing rate P-Rate=MHR+20 bpm is established in step 935 on the assumption that the patient's intrinsic heart rate is more likely to increase and should be overdriven more aggressively to avoid parasystole. The interference state pacing rate is augmented by 10 bpm (P-Rate=MHR+10 bpm) in step 945 on the assumption that the patient's intrinsic heart rate need not be overdriven as aggressively for the duration of the interference state to avoid parasystole.

PGPUB-DOCUMENT-NUMBER: 20030140933

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030140933 A1

TITLE: Process and apparatus for the removal of toxic components of tobacco smoke and the standardization of the health hazards related to those components

PUBLICATION-DATE: July 31, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Eichel, Bertram	Framingham	MA	US	

APPL-NO: 09/ 943144

DATE FILED: August 30, 2001

US-CL-CURRENT: 131/334

ABSTRACT:

The oral cavity is a source of sensitive biomarkers that allow the development of novel tobacco filters to reverse and eliminate acute adverse effects of tobacco smoke. Useful biomarkers are ubiquitous functional leukocytes and associated essential biochemical mechanisms, including metabolic pathways and specific enzymes, such as myeloperoxidase contained in fluid-cell lavages obtained from the human mouth. These biomarkers derived from the human mouth and sputum from the human respiratory system can be used to evaluate long-term chronic effects of tobacco smoke. A tobacco filter comprising strongly basic anion exchange resins and strongly acidic cation exchange resins with or without activated carbon, is used to detect, reduce and eliminate toxic substances from tobacco smoke while retaining taste and aroma. The novel filter in conjunction with biomarkers allow the establishment of performance standards that permit the direct visualization and measurement of acute adverse reactions caused by tobacco smoke. The measurement of these adverse effects allow a human health hazard reduction scale to be created to inform smokers of the relative "safety" of any smoking product.

---------- KWIC --------

Detail Description Paragraph - DETX (118):

[0121] In contrast to the above nordihydroguaiaretic acid effect upon myeloperoxidase, Tappel and Marr (1954) showed that 2.7.times.10.sup.-4 Molar (80 ppm) nordihydroguaiaretic acid produced seventy-one (71) percent inhibition of turnip peroxidase, fifty-six (56) percent inhibition of liver catalase (like myeloperoxidase, both heme enzymes) and seventy-one (71) percent inhibition of yeast alcohol dehydrogenase; while 2.7.times.10.sup.-3 Molar nordihydroguaiaretic acid (160 ppm) produced one hundred (100) percent inhibition of squash ascorbic acid oxidase (a copper enzyme), ninety-three (93) percent inhibition of rat liver cyclophorase, ninety-nine (99) percent **inhibition of pig heart D-amino acid oxidase, (a flavoprotein), seventy (70) percent inhibition** of rat liver cyclophorase, and ninety-nine (99) percent inhibition of jack bean urease. Nordihydroguaiaretic acid also is a well-known inhibitor of plant lipoxidase-catalyzed oxidation and auto-oxidation of

linoleate, Tappel et al. (1953). In still other experiments, Eichel (unpublished) found that nordihydroguaiaretic acid is an effective inhibitor of the respiratory chain including both succinic oxidase and reduced nicotinamide-adenine dinucleotide oxidase of mouse heart homogenates under certain conditions. The respiratory chain includes the cytochromes and cytochrome oxidase (known heme enzymes).

PGPUB-DOCUMENT-NUMBER: 20020198231

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020198231 A1

TITLE: Compositions and methods for the treatment of Parkinson's disease

PUBLICATION-DATE: December 26, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Nelson, Jodi	Denver	CO	US	

APPL-NO: 10/ 192414

DATE FILED: July 9, 2002

RELATED-US-APPL-DATA:

child 10192414 A1 20020709

parent continuation-in-part-of 09615639 20000713 US GRANTED

parent-patent 6417177 US

non-provisional-of-provisional 60143767 19990713 US

non-provisional-of-provisional 60175051 20000107 US

non-provisional-of-provisional 60202140 20000505 US

US-CL-CURRENT: 514/313

ABSTRACT:

This invention provides compositions and methods for increasing cellular respiration of melanized catecholamine neurons, and methods for alleviating symptoms or stopping appearance and/or progression of symptoms of Parkinson's disease and related conditions, characterized by nigrostriatal degeneration. An effective amount of a neuromelanin-binding composition having a quinoline ring in a suitable pharmaceutical carrier is administered to patient in need of such treatment. Preferably the composition comprises (-)-chloroquine. Selected adjuvants are also provided as part of the compositions of this invention.

[0001] This application is a continuation-in-part of U.S. patent application Ser. No. 09,615,639 filed Jul. 13, 2000, which takes priority from U.S. patent application Ser. No. 60/143,767 filed Jul. 13, 1999, U.S. patent application Ser. No. 60/175,051 filed Jan. 7, 2000, and U.S. patent application Ser. No. 60/202,140 filed May 5, 2000. All of the foregoing applications are incorporated herein by reference to the extent not inconsistent herewith.

---------- KWIC --------

Summary of Invention Paragraph - BSTX (121):

[0118] Enhancing agents are agents, which act to increase levels of active ingredient in the brain or to increase dopamine levels in the brain. Preferred enhancing agents are histamine (H.sub.1) receptor antagonists. These act to counteract increased histamine bioavailability resulting from active ingredient, especially CQ, inhibition of histamine methyltransferase (HMT) and diamine oxidase (DAO, the two primary degradative histamine pathways by chloroquine, and to minimize histamine-associated adverse events, which have been observed with antimalarial treatment formulas.

PGPUB-DOCUMENT-NUMBER: 20020192766

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020192766 A1

TITLE: Esterase free enzymes

PUBLICATION-DATE: December 19, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Reichert, Arno	Innsbruck		AT	
Riethorst, Waander	Breitenbach a. Inn		AT	
Knauseder, Franz	Kirchbichl		AT	
Palma, Norbert	Breitenbach a. Inn		AT	

APPL-NO: 10/ 216882

DATE FILED: August 12, 2002

RELATED-US-APPL-DATA:

child 10216882 A1 20020812

parent division-of 09508030 20000403 US GRANTED

parent-patent 6465227 US

child 09508030 20000403 US

parent a-371-of-international PCT/EP98/05729 19980908 WO UNKNOWN

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
AT	1505/97	1997AT-1505/97	September 9, 1997
AT	1506/97	1997AT-1506/97	September 9, 1997
AT	1507/97	1997AT-1507/97	September 9, 1997

US-CL-CURRENT: 435/71.1, 435/184 , 435/47

ABSTRACT:

A process for decreasing esterase activity present in the presence of D-amino acid oxidase activity or in the presence of glutarylacylase activity in a mixture having esterase activity and D-amino acid oxidase activity and/or having esterase activity and glutarylacylase activity by treatment with phenylmethylsulphonyl fluoride; immobilized biocatalyts in spherical particle form obtainable by treating microorganism cells having enzyme activity with a primary or secondary amine containing polymer, an organic solvent which is able to form a two-phase system with water and a bifunctional agent; and the use of that process and biocatalysts in the production of 7-aminocephalo-sporanic acid, 7-amino-3-hydroxymethyl-3-cep- hem-4-carboxylic acid and cephalosporin antibiotics.

---------- KWIC ---------

Summary of Invention Paragraph - BSTX (3):

[0003] It was now surprisingly found that the treatment of a mixture having esterase activity in the presence of DAO activity or having esterase activity in the presence of GAC activity with phenylmethylsulphonyl fluoride (PMSF) may decrease esterase activity considerably, e.g. substantially complete, whereas DAO, or GAC activity, respectively may remain high, e.g. substantially unchanged. This finding is surprising because according to the present invention PMSF, known e.g. as an irreversible inhibitor of serine containing proteins by serine sulphonylation, may decrease esterase activity present in the presence of DAO activity or in the presence of GAC activity selectively without, e.g. substantial influence on **DAO or GAC activity; and even more surprising is the selective and effective inhibition** by PMSF of esterase activity present in the presence of GAC activity, e.g. because of similar function and structure of acylases and esterases.

PGPUB-DOCUMENT-NUMBER: 20020048812

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020048812 A1

TITLE: Isolation and in vitro differentiation of conditionally immortalized murine olfactory receptor neurons

PUBLICATION-DATE: April 25, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Ronnett, Gabriele V.	Lutherville	MD	US	
Barber, Robert Duncan	Baltimore	MD	US	
Yau, King-Wai	Baltimore	MD	US	

APPL-NO: 09/ 758257

DATE FILED: January 12, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60176451 20000114 US

US-CL-CURRENT: 435/368, 435/325

ABSTRACT:

Olfactory receptor cell lines are conditionally immortalized. Under permissive conditions they proliferate. Under nonpermissive conditions the cells differentiate into mature functional Olfactory Receptor Neurons (ORNs) expressing multiple olfactory neuron-specific markers. Exposure of cells of the clonal lines to a battery of odorants indicates a functionally heterogeneous population, in which approximately 1% of the cells respond to any particular single odorant. This heterogeneity suggests the potential of the cells of the cell line to express multiple different receptors and demonstrates that the cell line is an appropriate model for native Olfactory Receptor Neurons.

[0001] This application claims the benefit of provisional application Ser. No. 60/176,451 filed Jan. 14, 2000. The text of the provisional application is incorporated herein by reference.

---------- KWIC ---------

Detail Description Paragraph - DETX (51):

[0083] To keep the amount of expressed TAg to the minimum required for immortalization (Noble et al., 1995), heterozygous offspring from homozygous male H-2K.sup.b-tsA58 transgenic and C57B1 female mice (Charles River Laboratories, Wilmington Mass., and Jackson Laboratory, Bar Harbor, Me., respectively) were used to generate the conditionally immortal neuronal cell culture. Cells were isolated in a procedure modified from a previously established technique (Ronnett et al., 1991). Briefly, post-natal day 1-3 animals were decapitated and the heads were sectioned longitudinally. The

olfactory epithelium and nasal septum were removed and placed in an Eppendorf tube containing 500 .mu.l culture medium. The culture medium consisted of Minimum Essential Medium in which the L-valine has been replaced by D-valine (MDV). This was supplemented with 10% fetal bovine serum (FBS), 4 mM glutamine, kanamycin (100 .mu.g.ml.sup.-1), gentamicin (50 U.ml.sup.-1) and amphotericin B (2.5 .mu.g.ml.sup.-1; all from Gibco BRL, Gaithersburg, Md.). The MDV medium was chosen because fibroblasts lack D-amino acid oxidase and the reduction of L-valine inhibits fibroblast survival and growth (Gilbert et al., 1986). Tissue was centrifuged at low speed for two minutes and then most of the medium was removed. The cell pellet was chopped briefly with a pair of fine-point scissors before being resuspended in supplemented cell culture medium. The resultant cell clumps and cell suspension were plated out onto 2- or 4-chamber glass slides (Nunc, Naperville, Ill.) or plastic dishes (Fisher Scientific, Pittsburgh, Pa.). To enhance ORN adhesion, all cell culture materials were pretreated with laminin (0.125 mg.ml.sup.-1 in serum-free media, Collaborative Biomedical Products, Bedford, Mass.) for at least 12 hours, prior to plating. Cells were maintained in culture at 33.degree. C. (the permissive temperature for the SV40 TAg) and, to stimulate transcription of the transgene, the culture medium was supplemented with murine .gamma.-interferon (40 U.ml.sup.-1, Genzyme, Cambridge, Mass.). Provisionally, in permissive conditions, the cell culture medium was supplemented with epidermal growth factor (EGF, 20 ng.ml.sup.-1, Gibco BRL) and 2.5 S nerve growth factor (NGF, 10 ng.ml.sup.-1, Gibco BRL) before thorough characterizations of their effects were made in later experiments.

PGPUB-DOCUMENT-NUMBER: 20020006663

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020006663 A1

TITLE: p27 and p21 in gene therapies

PUBLICATION-DATE: January 17, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Scadden, David T.	Weston	MA	US	
Cheng, Tao	Newton	MA	US	

APPL-NO: 09/ 803687

DATE FILED: March 9, 2001

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60213627 20000623 US

non-provisional-of-provisional 60188120 20000309 US

US-CL-CURRENT: 435/455, 435/366

ABSTRACT:

The expansion of a population of stem cells or progenitor cells, or precursors thereof, may be accomplished by disrupting or inhibiting p21.sup.cip1/waf1 and/or p27, cyclin dependent kinase inhibitors. In the absence of p27 activity, progenitor cells move into the cell cycle and proliferate; whereas in the absence of p21 activity, stem cells move into the cell cycle and proliferate without losing their pluripotentiality (i.e., their ability to differentiate into the various cell lines found in the blood stream). Any type of stem cell or progenitor cell, or precursor thereof, including, but not limited to, hematopoietic, gastrointestinal, lung, neural, skin, muscle, cardiac muscle, renal, mesenchymal, embryonic, fetal, or liver cell may be used in accordance with the invention. The present invention provides a method of expanding a cell population, cells with decreased p27 and/or p21 activity, transgenic animals with a disrupted p27 and/or p21 gene, pharmaceutical compositions comprising the cells of the invention, and methods of using these cells in gene therapy (e.g., stem cell gene therapy) and bone marrow transplantation.

RELATIONED APPLICATIONS

[0001] The present application claims priority to co-pending provisional applications, U.S. Ser. No. 60/213,627, filed Jun. 23, 2000, and U.S. Ser. No. 60/188,120, filed Mar. 9, 2000, each of which is incorporated herein by reference in its entirety.

---------- KWIC ---------

Detail Description Paragraph - DETX (9):
[0046] Unlike p21, p27 is controlled by both translational and

posttranslational mechanisms (Hengst et al. "Translation control of p27Kip1 accumulation during the cell cycle" Science 271:1861-1864, 1996; Pagano et al. "Role of the ubiquitin-proteasome pathway in regulating abundance of the cyclin-dependent kinase inhibitor p27 [see comments]" Science 269:682-685, 1995; each of which is incorporated herein by reference). A role for p27 in hematopoiesis is supported by direct flow cytometric evidence for expression in primitive cells (Tong et al. "TGF-.beta.suppresses cell division of Go CD34+cells while maintaining primitive hematopoietic potential" Exp. Hematol. 26:684, 1998; incorporated herein by reference), expression in more mature progenitors (Taniguchi et al. "Expression of p21 (Cip1/Waf1/Sdi1) and p27(Kip1) cyclin-dependent kinase inhibitors during human hematopoiesis" Blood 93:4167-4178, 1999; Yaroslavskiy et al. "Subcellular and cell-cycle expression profiles of CDK-inhibitors in normal differentiating myeloid cells" Blood 93:2907-2917, 1999; each of which is incorporated herein by reference) and indirectly by improved retroviral transduction in the context of anti-sense p27 (Dao et al. "Reduction in levels of the cyclin-dependent kinase inhibitor p27(kip 1) coupled with transforming growth factor beta neutralization induces cell-cycle entry and increases retroviral transduction of primitive human hematopoietic cells [In Process Citation]" Proc. Natl. Acad. Sci. USA 95:13006-13011, 1998; incorporated herein by reference). As shown in the Examples below, disruption of the p27 gene allows for expansion of a population of progenitor cells in vivo as well as ex vivo. In terms of gene therapy, a minority population of stem cells with less than wild type p27 activity tends to predominate the progenitor and mature blood cell compartments without leading to leukemia and polycythemia.

US-PAT-NO: 6796312

DOCUMENT-IDENTIFIER: US 6796312 B2

TITLE: Process and apparatus for the removal of toxic components of tobacco smoke and the standardization of the health hazards related to those components

DATE-ISSUED: September 28, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Eichel; Bertram	Framingham	MA	01701	N/A

APPL-NO: 09/ 943144

DATE FILED: August 30, 2001

US-CL-CURRENT: 131/334, 131/202 , 131/207 , 131/331 , 131/332

ABSTRACT:

The oral cavity is a source of sensitive biomarkers that allow the development of novel tobacco filters to reverse and eliminate acute adverse effects of tobacco smoke. Useful biomarkers are ubiquitous functional leukocytes and associated essential biochemical mechanisms, including metabolic pathways and specific enzymes, such as myeloperoxidase contained in fluid-cell lavages obtained from the human mouth. These biomarkers derived from the human mouth and sputum from the human respiratory system can be used to evaluate long-term chronic effects of tobacco smoke. A tobacco filter comprising strongly basic anion exchange resins and strongly acidic cation exchange resins with or without activated carbon, is used to detect, reduce and eliminate toxic substances from tobacco smoke while retaining taste and aroma. The novel filter in conjunction with biomarkers allow the establishment of performance standards that permit the direct visualization and measurement of acute adverse reactions caused by tobacco smoke. The measurement of these adverse effects allow a human health hazard reduction scale to be created to inform smokers of the relative "safety" of any smoking product.

27 Claims, 13 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 9

---------- KWIC ---------

Detailed Description Text - DETX (112):

In contrast to the above nordihydroguaiaretic acid effect upon myeloperoxidase, Tappel and Marr (1954) showed that 2.7.times.10.sup.-4 Molar (80 ppm) nordihydroguaiaretic acid produced seventy-one (71) percent inhibition of turnip peroxidase, fifty-six (56) percent inhibition of liver catalase (like myeloperoxidase, both heme enzymes) and seventy-one (71) percent inhibition of yeast alcohol dehydrogenase; while 2.7.times.10.sup.-3 Molar nordihydroguaiaretic acid (160 ppm) produced one hundred (100) percent inhibition of squash ascorbic acid oxidase (a copper enzyme), ninety-three (93)

percent inhibition of rat liver cyclophorase, ninety-nine (99) percent inhibition of pig heart D-amino acid oxidase, (a flavoprotein), seventy (70) percent inhibition of rat liver cyclophorase, and ninety-nine (99) percent inhibition of jack bean urease. Nordihydroguaiaretic acid also is a well-known inhibitor of plant lipoxidase-catalyzed oxidation and auto-oxidation of linoleate, Tappel et al. (1953). In still other experiments, Eichel (unpublished) found that nordihydroguaiaretic acid is an effective inhibitor of the respiratory chain including both succinic oxidase and reduced nicotinamide-adenine dinucleotide oxidase of mouse heart homogenates under certain conditions. The respiratory chain includes the cytochromes and cytochrome oxidase (known heme enzymes).

US-PAT-NO: 6465227

DOCUMENT-IDENTIFIER: US 6465227 B1
See image for Certificate of Correction

TITLE: Spherical particles containing microorganism cells having enzyme activity

DATE-ISSUED: October 15, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Reichert; Arno	Innsbruck	N/A	N/A	AT
Riethorst; Waander	Breitenbach a. Inn	N/A	N/A	AT
Knauseder; Franz	Kirchbichl	N/A	N/A	AT
Palma; Norbert	Breitenbach a. Inn	N/A	N/A	AT

APPL-NO: 09/ 508030

DATE FILED: April 3, 2000

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
AT	1505/97	September 9, 1997
AT	1506/97	September 9, 1997
AT	1507/97	September 9, 1997

PCT-DATA:
APPL-NO: PCT/EP98/05729
DATE-FILED: September 8, 1998
PUB-NO: WO99/13058
PUB-DATE: Mar 18, 1999
371-DATE: Apr 3, 2000
102(E)-DATE:Apr 3, 2000

US-CL-CURRENT: 435/180, 435/174 , 435/177 , 435/182

ABSTRACT:

A process is presented for producing spherical particles containing microorganism cells having desired enzyme activity. The process comprises the steps of mixing the cells directly with a primary or secondary amine-containing polymer, combining the resulting mixture with an organic solvent to form a two-phase system, and then adding a bifunctional cross-linking agent to yield the spherical particles. The preferred enzyme activities are D-amino acid oxidase and glutarylacylase activities.

4 Claims, 0 Drawing figures

Exemplary Claim Number: 1

---------- KWIC ---------

Brief Summary Text - BSTX (4):
It was now surprisingly found that the treatment of a mixture having esterase activity in the presence of DAO activity or having esterase activity

in the presence of GAC activity with phenyimethyisulphonyl fluoride (PMSF) may decrease esterase activity considerably, e.g. substantially complete, whereas DAO, or GAC activity, respectively may remain high, e.g. substantially unchanged. This finding is surprising because according to the present invention PMSF, known e.g. as an irreversible inhibitor of serine containing proteins by serine sulphonviation, may decrease esterase activity present in the presence of DAO activity or in the presence of GAC activity selectively without, e.g. substantial influence on DAO or GAC activity; and even more surprising is the selective and effective inhibition by PMSF of esterase activity present in the presence of GAC activity, e.g. because of similar function and structure of acylases and esterases.

US-PAT-NO: 5877013

DOCUMENT-IDENTIFIER: US 5877013 A

TITLE: Rhodosporidium D-amino acid oxidase

DATE-ISSUED: March 2, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Liao; Gwo-Jen	Taipei	N/A	N/A	TW
Lee; Yi-Jang	Hsinchu	N/A	N/A	TW
Lee; Yun-Huey	Kaohsiung	N/A	N/A	TW
Chen; Li-Lin	Hsinchu	N/A	N/A	TW
Chu; Wen-Shen	Hsinchu	N/A	N/A	TW

APPL-NO: 08/ 903624

DATE FILED: July 31, 1997

US-CL-CURRENT: 435/252.3, 435/189 , 435/320.1 , 536/23.2

ABSTRACT:

This invention relates to a D-amino acid oxidase of the genus Rhodosporidium and a gene encoding it.

6 Claims, 0 Drawing figures

Exemplary Claim Number: 1

---------- KWIC ---------

Detailed Description Text - DETX (15):

The relative activities of the purified DAO on various D-amino acid substrates were measured. The purified enzyme was active on all D-amino acids tested. The best substrate was D-tryptophan, followed by D-methionine, D-phenylalanine, D-alanine, and D-leucine. The enzyme exhibited less activity (<20% of maximal) for D-threonine, D-glutamic acid, D-aspartic acid, and D-lysine. No activity on L-amino acids, including L-alanine, L-proline, L-phenylalanine, and L-methionine, was detected. The apparent K.sub.m for each one of D-tryptophan, D-methionine, D-alanine and D-serine was 0.18 mM, 0.22 mM, 0.68 mM, and 3.4 mM, respectively. The enzyme was inhibited by 72%, 49%, and 21% in the presence of p-aminobenzoic acid, benzoic acid, and nicotinic acid, respectively. These aromatic acids were all determined to be competitive inhibitors for R. toruloides DAO. p-Aminobenzoic acid had the lowest K.sub.i (0.3 mM) among the aromatic acids tested.

US-PAT-NO: 5843303

DOCUMENT-IDENTIFIER: US 5843303 A

TITLE: Direct fired convection heating in residuum oil solvent extraction process

DATE-ISSUED: December 1, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ganeshan; Ram	Sugarland	TX	N/A	N/A

APPL-NO: 08/ 925211

DATE FILED: September 8, 1997

US-CL-CURRENT: 208/309, 201/14 , 201/15 , 208/320 , 208/427

ABSTRACT:

A residuum oil solvent extraction process is improved by using direct fired convection heaters for heating the asphaltene, the solvent-deasphalted oil phase, the deasphalted oil and the stripping steam, instead of hot oil heat exchangers. The convection heaters are fired using recirculated flue gas so that the hot flue gas supplied to the convection heaters has a temperature between 800.degree. F. and 1400.degree. F.

8 Claims, 3 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 2

---------- KWIC --------

Brief Summary Text - BSTX (10):

The present invention improves the residuum oil solvent extraction process by replacing the hot oil heating system with direct fired convection heating. This eliminates the hot oil piping, and reduces the number of pieces of equipment which are needed, particularly the heat exchangers. In turn, this eliminates all heat losses from the hot oil interconnect piping. The temperature of the flue gas can be reduced by recirculating the flue gas back to the combustion zone. This has the benefit of inhibiting deterioration of the process fluids (asphaltene, solvent-DAO and DAO phases) because the wall temperature of the tubes is lower. In addition, the diameter of the tubes in the convection heater are much larger, and dramatically reduce the likelihood of fouling or plugging of the diameter of the tubes. Milder operation enables better temperature control in the direct fired convection heater. Moreover, the levels of nitrogen oxide generated from the combustion of the fuel are lower because the temperature of the combustion products is lower in the direct fired heater due to recirculation of the cooled flue gases.

US-PAT-NO: 5677141

DOCUMENT-IDENTIFIER: US 5677141 A
See image for Certificate of Correction

TITLE: Process for producing 7-aminocephem compound or salts thereof

DATE-ISSUED: October 14, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Isogai; Takao	Ibaraki	N/A	N/A	JP
Fukagawa; Masao	Tsuchiura	N/A	N/A	JP
Iwami; Morita	Tsukuba	N/A	N/A	JP
Aramori; Ichiro	Kyoto	N/A	N/A	JP
Kojo; Hitoshi	Tsuchiura	N/A	N/A	JP

APPL-NO: 08/ 314309

DATE FILED: September 30, 1994

PARENT-CASE:

This is a continuation, of application Ser. No. 07/631,906 filed on Dec. 21, 1990, now abandoned.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
JP	1-341113	December 27, 1989
JP	2-193609	July 20, 1990

US-CL-CURRENT: 435/47, 435/256.4 , 435/51

ABSTRACT:

The present invention provides a process for producing 7-aminocephem compounds or salts thereof. 7-Aminocephem compounds are produced via microorganisms transformed with a vector containing a gene capable of converting a cephalosporin compound of the formula (II): ##STR1## to a 7-aminocephem compound of the formula (I): ##STR2##

11 Claims, 39 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 39

--------- KWIC --------

Detailed Description Text - DETX (262):
In the case of pDAO-EB101-carrying transformants, 500 .mu.l of a reactant solution containing 5 mg/ml CCNa, 0.1M phosphate buffer (pH 7.5) and 14 mM NaN.sub.3 and 5 .mu.l of toluene were added to centrifuged cells and the reaction was carried out at 37.degree. C. for 3 hours with shaking. NaN.sub.3 was added so that it could **inhibit catalase to thereby allow DAO**-catalyzed

conversion of CCNa to GL-7ACA without stopping at the stage of keto-AD-7ACA. In this way, 840 .mu.g/ml GL-7ACA was formed. In this case, it was also confirmed that transformants carrying pCYG-EB2 containing no DAO gene, which were used as controls, did not give GL-7ACA. It was thus found that the A. chrysogenum ATCC 11550-derived protease gene expression unit can function in S. cerevisiae YNN27, causing D-amino acid oxidase formation. It was also found that the F. solani M-0718-derived DAO cDNA cab be expressed in S. cerevisiae YNN27.

US-PAT-NO: 5610195

DOCUMENT-IDENTIFIER: US 5610195 A

TITLE: Ornithine decarboxylase inhibiting branched aminooxy amino alkane derivatives

DATE-ISSUED: March 11, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Frei; J org	H olstein	N/A	N/A	CH
Stanek; Jaroslav	Arlesheim	N/A	N/A	CH

APPL-NO: 08/ 351336

DATE FILED: December 12, 1994

PARENT-CASE:

This application is a 371 of PCT/EP94/01036, filed Apr. 4, 1994.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
CH	1129/93	April 13, 1993

PCT-DATA:
APPL-NO: PCT/EP94/01036
DATE-FILED: April 2, 1994
PUB-NO: WO94/24094
PUB-DATE: Oct 27, 1994
371-DATE: Dec 12, 1994
102(E)-DATE:Dec 12, 1994

US-CL-CURRENT: 514/645, 564/301

ABSTRACT:

Compounds of formula (I) in which (a) four of the radicals R.sub.1, R.sub.2, R.sub.3, R.sub.4, R.sub.5 and R.sub.6 are hydrogen and the others independently of one another are in each case C.sub.1 -C.sub.2 alkyl, these groups being bonded to the same carbon atom or to two different carbon atoms, or (b) five of the radicals R.sub.1, R.sub.2, R.sub.3, R.sub.4, R.sub.5 and R.sub.6 are hydrogen and the other radical is C.sub.1 -C.sub.2 alkyl or hydroxymethyl, or salts thereof, are described. The compounds of formula (I) and their salts are ornithine decarboxylase inhibitors.

39 Claims, 0 Drawing figures

Exemplary Claim Number: 1

---------- KWIC ---------

Brief Summary Text - BSTX (5):
In mammalian cells, ODC catalyses the synthesis of putrescine, an intermediate in polyamine biosynthesis. The breakdown of putrescine in the

cell is effected in particular by diamine oxidase (DAO). If the DAO is active, excess putrescine can be broken down, which further promotes the action of an ODC inhibitor. The less an inhibitor of ODC inhibits DAO, i.e. the higher its specificity, the more advantageous its properties.

Brief Summary Text - BSTX (9):
Compared with APA, the compounds of the present invention tested show, for example, an increased selectivity in the inhibition of ODC with respect to inhibition of DAO.

Brief Summary Text - BSTX (23):
The selectivity of the inhibition of ODC with respect to diamine oxidase (DAO) is demonstrated by the following test system (cf. Seppanen et al., in: Polyamines, Tabor, H., and White-Tabor, C. (editors), Methods Enzymol. 94, 274-253, Academic Press, New York & London 1983): DAO from pig kidney (obtainable from Sigma Chemie, Deisenhofen, Germany) is employed in particular as the enzyme instead of the enzyme from the rat small intestine. Briefly, the batch contains (expressed as the final concentrations) 0.1M potassium phosphate buffer pH 7.4; 10 mM mercaptoethanol, 0.40 mM putrescine, including 40 nCi [1,4-.sup.14 C]putrescine (Amersham, 110 Ci/mole) and variable amounts of enzyme protein (DAO) and inhibitor. For standard experiments, the batches are incubated for 30 minutes at 37.degree. C. and then transferred to an ice-bath. The reaction is stopped by addition of 0.5 ml of ice-cold 1M Na.sub.2 CO.sub.3 solution which contains 1 mM aminoguanidine. After addition of 4 ml of toluene with 5 g/l of PPO (2,5-diphenyloxazole), the test tube is continuously inverted around the transverse axis at room temperature for 10 minutes, for mixing, and is then centrifuged at 1800.times.g in a centrifugal rotor at 4.degree. C. for 5 minutes and finally frozen in ethanol/dry ice. The liquid upper phase is transferred to a scintillation glass, the frozen lower phase is thawed by incubation for 5 minutes at 37.degree. C., 4 ml of toluene/PPO are added again and the mixture is extracted again as above. After a total of 3 extractions, the combined toluene extracts (which contain the radiolabelled 1-pyrroline to the extent that it has been liberated from putrescine by the action of the DAO) are measured in a liquid scintillation counter (Rack Beta 1215, LKB-Wallac). For calculation of the radioactivity employed, an aliquot of the aqueous phase after 3 extractions is transferred to Whatman GF/C filter (glass fibre filter, Whatman, USA), dried in vacuo and, after addition of 5 ml of toluene/PPO, is counted. For determination of the extraction blank values, a control which contains 25 mM Tris/1 mm EDTA/1 mM dithiothreitol pH 7.4 instead of DAO is used in each test series. The inhibitor concentrations at which 50% inhibition exists compared with the non-inhibited DAO are determined from the linear regression of the log(inhibitor concentration) against the relative DAO activity (% of the non-inhibited control), only relative activities of between 95 and 5% being included in the calculation.

Brief Summary Text - BSTX (24):
The numerical ratio of the IC.sub.50 for the DAO inhibition to the IC.sub.50 for the ODC inhibition [quotient of IC.sub.50 (DAO)/IC.sub.50 (ODC)] is preferably more than 150 to about 800 for the compounds according to the invention, which demonstrates a high selectivity of inhibition of ODC with respect to DAO; in contrast, the corresponding quotient for APA is about 1.2

US-PAT-NO: 5284749

DOCUMENT-IDENTIFIER: US 5284749 A

TITLE: Diamine oxidase and assay for rupture of amniotic membrane in pregnant mammals

DATE-ISSUED: February 8, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cowley; David M.	Brisbane	N/A	N/A	AU
Maguire; David J.	Brisbane	N/A	N/A	AU
Voroteliak; Victor	Brisbane	N/A	N/A	AU

APPL-NO: 07/ 623168

DATE FILED: October 31, 1990

US-CL-CURRENT: 435/7.1, 436/501 , 436/514 , 436/518 , 436/536 , 436/548

ABSTRACT:

Assay for detection of a form of diamine oxidase which is present only in amniotic fluid and, more especially, for detection of amniotic membrane rupture by detection of the amniotic fluid diamine oxidase. The assay includes the steps of detecting the amniotic fluid diamine oxidase and distinguishing that from another form of diamine oxidase found in serum. The assay may be carried out on a sample of vaginal fluid from a pregnant female wherein the sample is subjected to the assay to detect the leakage or presence of amniotic fluid diamine oxidase. Purified forms of amniotic fluid diamine oxidase and serum diamine oxidase which is different from amniotic fluid diamine oxidase and found in serum are also described, together with a method of purifying both forms of diamine oxidase.

11 Claims, 14 Drawing figures

Exemplary Claim Number: 6

Number of Drawing Sheets: 14

---------- KWIC ---------

Detailed Description Text - DETX (154):
FIG. 1. Phosphate salt inhibition of amniotic fluid DAO (O) and maternal serum DAO (X). The increasing phosphate salt concentrations were substituted for the 1/15M phosphate buffer, pH 7.4, used in the radioenzymatic assay.

Detailed Description Text - DETX (155):
FIG. 2. Salt inhibition of amniotic fluid DAP (O) and maternal serum DAO (X). The increasing salt concentrations were prepared in the 1/15M phosphate buffer, pH 7.4, used in the radioenzymatic assay.

US-PAT-NO: 5190864

DOCUMENT-IDENTIFIER: US 5190864 A
See image for Certificate of Correction

TITLE: Enzyme amplification by using free enzyme to release enzyme from an immobilized enzyme material

DATE-ISSUED: March 2, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Giese; Roger W.	Quincy	MA	N/A	N/A
Ehrat; Markus	Suhr	N/A	N/A	CH
Cecchini; Douglas J.	Somerville	MA	N/A	N/A

DISCLAIMER DATE: 20070626

APPL-NO: 07/ 516321

DATE FILED: April 30, 1990

PARENT-CASE:

This application is a continuation of application Ser. No. 852,237, filed Apr. 15, 1986, now U.S. Pat. No. 4,937,188.

US-CL-CURRENT: 435/41, 435/174 , 435/176 , 435/177 , 435/178 , 435/181 , 435/183 , 435/4 , 435/7.9 , 435/7.92

ABSTRACT:

A method for amplifying enzyme activity is disclosed. Enzyme amplification is achieved by covalently bonding enzyme to a supporting material via a molecular chain which is a substrate for the enzyme, then introducing a small amount of enzyme in the free state to this system, causing release of a large amount of bound enzyme. In an alternative embodiment, complementary enzymatically inactive fragments of an active enzyme, which fragments can recombine to form active enzyme, are covalently attached to separate support materials by a molecular chain material which is a substrate for the active enzyme, and these two fragment-supported conjugates are connected in series. Upon application of free enzyme or free complementary enzyme to one of these fragment-support conjugates, followed by application of the resulting product mixture to the second fragment-support conjugate, a large amount of free enzyme is ultimately produced. In a second alternative embodiment, two different active enzymes are each attached to separate supporting materials by different leashes, in which the leash for the first enzyme only is cleaved in the system by the second enzyme, and the leash for the second enzyme only is cleaved in the system by the first enzyme. These two materials are connected in series, and upon application of the second enzyme to the first enzyme-support conjugate, followed by application of the released first enzyme to the second enzyme-support conjugate material, ultimately a large amount of released active second enzyme is produced. Also disclosed are molecular conjugates of enzyme material on supports, required for the enzyme amplification.

24 Claims, 8 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 8

---------- KWIC --------

Detailed Description Text - DETX (79):

In order to reduce residual RNase activity, the S-protein was purified twice over a uridine-5'-triphosphate agarose gel as described elsewhere (13). The enzymatic activity (RNA substrate) of the purified S-protein was 0.02% that of native RNase A compared to 0.2% before the affinity chromatography. Moreover, the coupling reaction between the PDP-S-protein and GMB-DAO-poly C, and the subsequent immobilization of the resulting product on Thiol-Sepharose-4B, were run in a 0.5M phosphate buffer. Phosphate competitively **inhibits RNase (11) and should retard the degradation of the DAO**-poly C by the residual RNase activity remaining in the affinity purified S-protein. The S-peptide contained less than 0.003% RNase activity and no further purification was attempted.

US-PAT-NO: 4997827

DOCUMENT-IDENTIFIER: US 4997827 A

TITLE: Compositions containing 5-.alpha.-dihydro-19-norethisterone and derivatives thereof for in vivo inhibition of aromatase

DATE-ISSUED: March 5, 1991

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Osawa; Yoshio	Buffalo	NY	N/A	N/A

DISCLAIMER DATE: 20060509

APPL-NO: 07/ 321083

DATE FILED: March 9, 1989

PARENT-CASE:

This is a Continuation-In-Part of U.S. Ser. No. 07/257,723 filed Oct. 14, 1988, which is a Continuation of U.S. Ser. No. 07/019,338 filed Feb. 26, 1987 now U.S. Pat. No. 4,829,059.

US-CL-CURRENT: 514/178, 435/184 , 552/592

ABSTRACT:

A composition for in vivo inhibition of aromatase in a mammal, which comprises an in vivo inhibitory amount of a compound having the following general formula: ##STR1## wherein R.sub.1 is hydrogen or C.sub.1-20 acyl, in combination with a pharmaceutically acceptable carrier or diluent thereof.

22 Claims, 16 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 15

---------- KWIC ---------

Detailed Description Text - DETX (16):

A single injection of 5.alpha.-DHNET (50 mg/kg body weight) to normal 4-day cycling rats caused a cessation of the estrus cycle for 4 to 6 cycles (16 to 24 days), whereas the sesame oil-only controls and a group treated with the same dose of 6.beta.-bromoandrostenedione, a potent in vitro aromatase inhibitor (R. M. Budnick & T. L. Dao, Steroids, 35, 533-541 (1980); S. J. Santner, H. Rosen, Y. Osawa and R. J. Santen, J. Steroid Biochem. 20, 1239-1242 (1984); Y. Osawa, M. J. Coon and Y. Osawa, Fed. Proc., 45, 1749, A-1564 (1986)) showed no effect on the cycle, as shown in Example 1. The four-day treatment of 4-day cycling rats with 5.alpha.-DHNET showed, as exhibited in Example 2, a significant 67% suppression (p<0.0005) of the ovarian aromatase activity. The in vivo action of 5.alpha.-DHNET was compared to those of 6.alpha.-bromoandrostenedione (only insignificant 10% suppression) and 6.beta.-bromoandrostenedione (72%

suppression), both of which are potent in vivo aromatase inhibitors as shown in the references cited above.

US-PAT-NO: 4978658

DOCUMENT-IDENTIFIER: US 4978658 A

TITLE: Compositions containing 5.alpha.-dihydro-19-norethisterone and derivatives thereof for in vivo inhibition of aromatase

DATE-ISSUED: December 18, 1990

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Osawa; Yoshio	Buffalo	NY	N/A	N/A

APPL-NO: 07/ 257723

DATE FILED: October 14, 1988

PARENT-CASE:

This is a continuation of application Ser. No. 07/019,338, filed Feb. 26, 1987, now U.S. Pat. No. 4,829,059.

US-CL-CURRENT: 514/178, 552/649

ABSTRACT:

A composition for in vivo inhibition of aromatase in a mammal, which comprises an in vivo inhibitory amount of a compound having the following general formula: ##STR1## wherein R.sub.1 is hydrogen or C.sub.1-4 acyl, in combination with as pharmaceutically acceptable carrier or diluent thereof.

14 Claims, 14 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 14

---------- KWIC ---------

Detailed Description Text - DETX (14):

A single injection of 5.alpha.-DHNET (50 mg/kg body weight) to normal 4-day cycling rats caused a cessation of the estrus cycle for 4 to 6 cycles (16 to 24 days), whereas the sesame oil-only controls and a group treated with the same dose of 6.beta.-bromoandrostenedione, a potent in vitro aromatase inhibitor (R. M. Budnick & T. L. Dao, Steroids, 35, 533-541 (1980); S. J. Santner, H. Rosen, Y. Osawa and R. J. Santen, J. Steroid Biochem. 20, 1239-1242 (1984); Y. Osawa, M. J. Coon and Y. Osawa, Fed. Proc., 45, 1749, A-1564 (1986)) showed no effect on the cycle, as shown in Example 1. The four-day treatment of 4-day cycling rats with 5.alpha.-DHNET showed, as exhibited in Example 2, a significant 67% suppression (p<0.0005) of the ovarian aromatase activity. The in vivo action of 5.alpha.-DHNET was compared to those of 6.alpha.-bromoandrostenedione (only insignificant 10% suppression) and 6.beta.-bromoandrostenedione (72% suppression), both of which are potent in vitro aromatase inhibitors as shown in the references cited above.

US-PAT-NO: 4937188

DOCUMENT-IDENTIFIER: US 4937188 A

TITLE: Enzyme activity amplification method for increasing assay sensitivity

DATE-ISSUED: June 26, 1990

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Giese; Roger W.	Quincy	MA	N/A	N/A
Ehrat; Markus	Suhr	N/A	N/A	CH
Cecchini; Douglas J.	Somerville	MA	N/A	N/A

APPL-NO: 06/ 852237

DATE FILED: April 15, 1986

US-CL-CURRENT: 435/41, 435/174 , 435/177 , 435/181 , 435/4 , 435/7.9 , 435/7.92 , 435/962 , 435/966

ABSTRACT:

Enzyme amplification is achieved by covalently bonding enzyme to a supporting material via a molecular chain which is a substrate for the enzyme, then introducing a small amount of enzyme in the free state to this system, causing release of a large amount of bound enzyme. In an alternative embodiment, complementary enzymatically inactive fragments of an active enzyme, which fragments can recombine to form active enzyme, are covalently attached to separate support materials by a molecular chain material which is a substrate for the active enzyme, and these two fragment-support conjugates are connected in series. Upon application of free enzyme or free complementary enzyme to one of these fragment-support conjugates, followed by application of the resulting product mixture to the second fragment-support conjugate, a large amount of free enzyme is ultimately produced. In a second alternative embodiment, two different active enzymes are each attached to separate supporting materials by different leashes, in which the leash for the first enzyme only is cleaved in the system by the second enzyme, and the leash for the second enzyme only is cleaved in the system by the first enzyme. These two materials are connected in series, and upon application of the second enzyme to the first enzyme-support conjugate, followed by application of the released first enzyme to the second enzyme-support conjgate material, ultimately a large amount of released active second enzyme is produced. The amplification of enzyme activity has uses in analytical chemistry such as to increase sensitivity of a standard immunoassay.

40 Claims, 9 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 8

---------- KWIC ---------

Detailed Description Text - DETX (79):

In order to reduce residual RNase activity, the S-protein was purified twice over a uridine-5'-triphosphate agarose gel as described elsewhere (13). The enzymatic activity (RNA substrate) of the purified S-protein was 0.02% that of native RNase A compared to 0.2% before the affinity chromatography. Moreover, the coupling reaction between the PDP-S-protein and GMB-DAO-poly C, and the subsequent immobilization of the resulting product on Thiol-Sepharose-4B, were run in a 0.5M phosphate buffer. Phosphate competitively inhibits RNase (11) and should retard the degradation of the DAO-poly C by the residual RNase activity remaining in the affinity purified S-protein. The S-peptide contained less than 0.003% RNase activity and no further purification was attempted.

US-PAT-NO: 4888283

DOCUMENT-IDENTIFIER: US 4888283 A

TITLE: Selective inhibitors of benzylaminoxidases with respect to other aminoxidases

DATE-ISSUED: December 19, 1989

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bertini; Vincenzo	Cosenza	N/A	N/A	IT
De Munno; Angela	Pisa	N/A	N/A	IT
Lucchesini; Francesco	Rende	N/A	N/A	IT
Buffoni; Franca	Florence	N/A	N/A	IT
Bertocci; Barbara	Pistoia	N/A	N/A	IT

APPL-NO: 07/ 193236

DATE FILED: May 11, 1988

PARENT-CASE:

This application is a division of application Ser. No. 846,681, filed Apr. 1, 1986.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
IT	47906 A/85	April 1, 1985

US-CL-CURRENT: 435/184, 435/189 , 564/388 , 564/389 , 564/390 , 564/391

ABSTRACT:

Selective inhibitors of benzylaminoxidases, said inhibitors consisting of compounds of the general formula I ##STR1## wherein X is a group C--R.sup.4 or a nitrogen atom, R.sup.1 and R.sup.2, which can be the same or different from each other, represent hydrogen, hydroxyl groups, alkoxyl groups, or alkyl, alkenyl, hydroxyalkyl, alkoxyalkyl, hydroxyalkoxyalkyl, hydroxyalkoxyl, alkoxyalkoxyl, hydroxyalkoxyalkoxyl, phenoxyl or phenoxyalkyl groups or their substitution derivatives in the phenoxyl group, provided that no more than one of the same be hydrogen, and one or more of the symbols R.sup.3, R.sup.4 or R.sup.5 are hydrogen atoms or alkyl or hydroxyl or alkoxyl or hydroxyalkyl or hydroxyalkoxyl or hydroxyalkoxyalkyl or haloalkyl or carbonyl or carboxylic or ester or amido or nitrile or sulfonic groups or halogen atoms or nitro groups.

11 Claims, 0 Drawing figures

Exemplary Claim Number: 1

---------- KWIC ---------

Brief Summary Text - BSTX (2):

More particularly, this invention relates to organic compounds suitable for causing the selective **inhibition of benzylaminoxidases (BAO) with respect to diaminoxidases (DAO)**, to lysyloxidases (LAO) and to monoaminoxidases of the A

and the B types [MAO (A), MAO (B)].

Brief Summary Text - BSTX (36):

The inhibitors which are the object of the present invention can reach very high inhibition powers towards benzylaminoxidases (BAO's), with IC.sub.50 (M) values of the order of 10.sup.-7, whereas the same compounds **inhibit the aminooxidases DAO**, LAO, MAO (A) and MAO (B) just at quite a low degree, showing IC.sub.50 (M) values which are about 10.sup.4 -10.sup.5 times greater than those relevant to BAO.

US-PAT-NO: 4879306

DOCUMENT-IDENTIFIER: US 4879306 A

TITLE: Composition killing or inhibiting the growth of microorganisms and the use thereof

DATE-ISSUED: November 7, 1989

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Henkels; Wolf-Dieter	Edingen-Neckarh	N/A	N/A	DE
Balzer; Marion	Neckarbischofsheim	N/A	N/A	DE

APPL-NO: 06/ 780784

DATE FILED: September 27, 1985

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
DE	3436989	October 9, 1984

US-CL-CURRENT: 514/441, 162/161 , 210/764 , 514/528

ABSTRACT:

A composition killing or inhibiting the growth of microorganisms is described and which contains a mixture of 4,5-dichloro-1,2-dithiol-3-one and dibromonitrilopropionamide. The combination leads to a marked synergistic action of the two active substance components in the control of microorganisms. The composition is suitable for use in a large number of industrial systems.

8 Claims, 3 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 3

---------- KWIC ---------

Detailed Description Text - DETX (5):

(c) The results are given in Table 1, in which Q.sub.a and Q.sub.b are the minimum inhibiting concentration of DDQ or DBNPA in ppm when used alone, whilst Q.sub.A and Q.sub.B give the weight proportion of the particular active substance in the corresponding dilution stage containing the minimum inhibiting concentration of the mixture.

US-PAT-NO: 4829059

DOCUMENT-IDENTIFIER: US 4829059 A

TITLE: Compositions containing 5.alpha.-dihydro-19-norethisterone for in vivo inhibition of endocrine-dependent conditions in mammals

DATE-ISSUED: May 9, 1989

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Osawa; Yoshio	Buffalo	NY	N/A	N/A

APPL-NO: 07/ 019338

DATE FILED: February 26, 1987

US-CL-CURRENT: 514/178

ABSTRACT:

A composition for in vivo inhibition of aromatase in a mammal, which comprises an in vivo inhibitory amount of a compound having the following general formula: ##STR1## wherein R.sub.1 is hydrogen or C.sub.1-4 acyl, in combination with a pharmaceutically acceptable carrier or diluent thereof.

11 Claims, 14 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 14

---------- KWIC --------

Detailed Description Text - DETX (14):

A single injection of 5.alpha.-DHNET (50 mg/kg body weight) to normal 4-day cycling rats caused a cessation of the estrus cycle for 4 to 6 cycles (16 to 24 days), whereas the sesame oil-only controls and a group treated with the same dose of 6.beta.-bromoandrostenedione, a potent in vitro aromatase inhibitor (R. M. Budnick & T. L. Dao, Steroids, 35, 533-541 (1980); S. J. Santner, H. Rosen, Y. Osawa and R. J. Santen, J. Steroid Biochem. 20, 1239-1242 (1984); Y. Osawa, M. J. Coon and Y. Osawa, Fed. Proc., 45, 1749, A-1564 (1986)) showed no effect on the cycle, as shown in Example 1. The four-day treatment of 4-day cycling rats with 5.alpha.-DHNET showed, as exhibited in Example 2, a significant 67% suppression (p<0.0005) of the ovarian aromatase activity. The in vivo action of 5.alpha.-DHNET was compared to those of 6.alpha.-bromoandrostenedione (only insignificant 10% suppression) and 6.beta.-bromoandrostenedione (72% suppression), both of which are potent in vitro aromatase inhibitors as shown in the references cited above.

US-PAT-NO: 4635211

DOCUMENT-IDENTIFIER: US 4635211 A

TITLE: Speech synthesizer integrated circuit

DATE-ISSUED: January 6, 1987

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Yoshida; Hideo	Kashihara	N/A	N/A	JP
Kunita; Hisao	Yamatokoriyama	N/A	N/A	JP

APPL-NO: 06/ 434500

DATE FILED: October 15, 1982

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
JP	56-169337	October 21, 1981
JP	56-169338	October 21, 1981
JP	56-169339	October 21, 1981
JP	56-175103	October 30, 1981

US-CL-CURRENT: 704/270, 704/258

ABSTRACT:

Disclosed is a speech synthesizer integrated circuit as a preferred embodiment of the present invention, which is characterized in that;

Using one chip LSI, it implements the fundamental controls for the speech synthesizing operations, for example, and fundamental controls for the key input and display operations (corresponding to the functions usually performed by any of the conventional microprocessors). The preferred embodiment of the present invention has made it possible to realize an extremely useful and versatile speech synthesizer integrated circuit by externally connecting a memory that stores the controlled programs and sound data available for synthesizing the intended speech. By allocating the same addresses to the internal and external memory storage areas, programs can be located at identical memory addresses, thereby increasing system efficiency.

19 Claims, 7 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 5

---------- KWIC ---------

Detailed Description Text - DETX (47):

The preferred embodiment of the present invention provides a control circuit that controls the input of the D/A converter circuit as shown in FIG. 6, and as a result, unwanted power dissipation can be prevented. In other words, when the Amp signal is low, the analog switch AS turns off and the input to the inverter circuit A becomes high. Then, DAo becomes low, inhibiting the current

to flow through the feedback resistor FR.

US-PAT-NO: 4567000

DOCUMENT-IDENTIFIER: US 4567000 A
See image for Certificate of Correction

TITLE: 11-Difluoromethylene steroids

DATE-ISSUED: January 28, 1986

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ayer; Donald E.	Kalamazoo	MI	N/A	N/A

APPL-NO: 06/ 646605

DATE FILED: August 31, 1984

US-CL-CURRENT: 552/520, 552/526 , 552/621 , 987/160

ABSTRACT:

11-Difluoromethylene steroids having progestational and anti-progestational properties, useful as anti-fertility agents, are disclosed as well as a process for making the 11-difluoromethylene steroids.

24 Claims, 0 Drawing figures

Exemplary Claim Number: 1,15

---------- KWIC --------

Brief Summary Text - BSTX (34):
The 11-difluoromethylene steroids (VIII, X, XI, XV and XVI) useful as female contraceptive agents are those with anti-progestational activity, i.e., those compounds which **inhibit the action of progesterone in the following tests: DAO,** nuclear translocation, expression of uteroglobin gene, and most importantly interruption of pregnancy in laboratory animals as is well known to those skilled in the art, see for DAO assay supra. The female contraceptive steroids are administered such that the female mammal receives about 0.01 to about 1.0 mg/kg/day. For a 50 kg female, the amount would be about 0.5 to about 50 mg/day.

Detailed Description Paragraph Table - DETL (1):
TABLE 1

Compound	Rabbit	Rat	Dose (.mu.g)	BP	RBA.sup.1 (%)	DAO.sup.2
11-Difluoromethylene-17.beta.-hydroxy-17.alpha.-(1-propynyl)-estr-4-en-3-one	82	269	10	117	50	29
	100	19	200	15		
11-Difluoromethylene-13-ethyl-17.beta.-hydroxy-17.alpha.-(1-propynyl)-gon-4-en-3-one	104	Not run	Not run			

.sup.1 Relative Binding Affinity, progesterone = 100% .sup.2 Diamine oxidase; when biopotency (BP) value is 0, the test completely **inhibits the progesterone induced DAO.** When the value is 100, the test compound does not give any inhibition of progesterone induced DA enzyme. The lower the value the greater the antiprogestin activity of the test compound.

US-PAT-NO: 4557867

DOCUMENT-IDENTIFIER: US 4557867 A
See image for Certificate of Correction

TITLE: 11.beta.-Difluoromethyl and (E)- and (Z)-11-fluoromethylene steriods

DATE-ISSUED: December 10, 1985

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Campbell; J. Allan	Kalamazoo	MI	N/A	N/A

APPL-NO: 06/ 639285

DATE FILED: August 8, 1984

PARENT-CASE:

BACKGROUND OF THE INVENTION

The present application is a continuation-in-part of co-pending application Ser. No. 573,787, filed Jan. 25, 1984 which was a continuation-in-part of U.S. patent application Ser. No. 561,605 filed Dec. 14, 1983, both now abandoned.

US-CL-CURRENT: 540/30, 540/10 , 540/31 , 540/34 , 552/526 , 552/539 , 552/621 , 552/646 , 552/647

ABSTRACT:

Known reactions are arranged in a novel manner to produce 11.beta.-difluoromethyl and (E)- and (Z)-11-fluoromethylene 19-norandrostenediones and 19-nor-13.beta.-ethylandrostenediones which are useful as contraceptive agents.

12 Claims, 0 Drawing figures

Exemplary Claim Number: 5,6

---------- KWIC --------

Brief Summary Text - BSTX (49):

The 11.beta.-difluoromethyl steroids (VII, VIII, XVII and XVIII) useful as female contraceptive agents are those 11.beta.-difluoromethyl steroids (VII, VIII, XVII and XVIII) with anti-progestational activity, i.e., those compounds which inhibit the action of progesterone in the following tests: DAO, nuclear translocation, expression of uteroglobin gene, and most importantly interruption of pregnancy in laboratory animals as is well known to those skilled in the art, see for DAO assay supra. Those 11.beta.-difluoromethyl steroids (VII, VIII, XVII and XVIII) are administered such that the female mammal receives about 0.01 to about 1.0 mg/kg/day. For a 50 kg female, the amount would be about 0.5 to about 50 mg/day.

Detailed Description Text - DETX (242):

In the DAO (diamine oxidase) assay when the BP (biopotency) value is 0, the test compound completely inhibits the progesterone induced DAO. When the value is 100 the test compound does not give any inhibition of the progesterone induced DAO enzyme. The lower the value the greater the antiprogestin activity of the test compound.

Detailed Description Paragraph Table - DETL (1):

TABLE 1 Relative DAO Binding Assay

Affinity'	B.P.	Compound (%) (Dose in mg)
11.beta.-Difluoromethyl-17.beta.-hydroxyestr-	13	4-en-3-one
17.alpha.-Ethynyl-11.beta.-difluoromethyl-17.beta.-	92	6 (.1)
hydroxyestr-4-ene-3-one 3-ethane-		dithiol ketal
11.beta.-Difluoromethyl-17.beta.-hydroxy-17.alpha.-	68	8 (.1)
propynylestr-4-en-3-one (E)-11-fluoromethylene-17.beta.-hydroxy-	18	8 (.006)
17.alpha.-propynylestr-4-ene-3-one 11.beta.-Difluoromethyl-17.beta.-hydroxy-		
3	8	(.2*) 17.alpha.-propynylestr-4-ene
11.beta.-Difluoromethyl-17.beta.-hydroxy-	2	17.alpha.-propynylestr-3-ene
17.alpha.-Ethynyl-11.beta.-difluoromethyl-	2	0 (.2*)
17.beta.-hydroxyestr-4-ene 11.beta.-Difluoromethyl-17.beta.-hydroxyestr-	66	
4-en-3-one 17-methyl 17.alpha.-Ethynyl-11.beta.-difluoromethyl-	145	69 (.05*)
17.beta.-hydroxyestr-4-en-3-one 17-methyl ether		
11.beta.-Difluoromethyl-17.beta.-hydroxy-	90	206 (.05*)
17.alpha.-propynylestr-4-en-3-one 17-methyl ether		
17.alpha.-Ethynyl-11.beta.-difluoromethyl-	50	129 (.05)
17.beta.-hydroxyestr-4-en-3-one 17-acetate		
11.beta.-Difluoromethyl-17.beta.-hydroxy-	49	14 (.05)
17.alpha.-propynylestr-4-en-3-one 17-acetate		
17.alpha.-Ethynyl-(E)-11-fluoromethylene-	74	0 (.0125)
17.beta.-hydroxyestr-4-en-3-one (E)-11-Fluoromethylene-17.beta.-hydroxy-	71	
54 (.2) 17.alpha.-propynylestr-4-en-3-one 17-methyl ether		
(E)-11-Fluoromethylene-17.beta.-hydroxy-	58	0 (.0125)
7.alpha.-methyl-17.alpha.-propynylestr-4-		en-3-one
11.beta.-Difluoromethyl-17.beta.-hydroxy-	41	0 (.05*)
7.alpha.-methyl-17.alpha.-propynylestr-4-		en-3-one
17.alpha.-Ethynyl-(E)-11-fluoromethylene-	34	0 (.125)
17.beta.-hydroxy-7.alpha.-methylestr-		4-en-3-one
17.alpha.-Ethynyl-11.beta.-difluoromethyl-	63	0 (.05*)
17.beta.-hydroxy-7.alpha.-methylestr-		4-en-3-one
13.beta.-Ethyl-(E)-11-fluoromethylene-	63	>100 (.07)
17.beta.-hydroxy-17.alpha.-propynylgon-		4-en-3-one
(Z)-11-Fluoromethylene-17.beta.-	150	100 (.01) hydroxy-17-propynylestr-4-en-
3-one 17.alpha.-Ethynyl-(Z)-11-fluoromethylene-	149	100 (.01)
17.beta.-hydroxyestr-4-en-3-one 13.beta.-Ethyl-(Z)-11-fluoromethylene-	149	
17.beta.-hydroxy-17.alpha.-propynylgon-4-		en-3-one
13.beta.-Ethyl-17.alpha.-ethynyl-(E)-11-	100	
fluoromethylene-17.beta.-hydroxygon-		4-en-3-one

*Minimum dose to give near complete inhibition of DAO not yet determined.

US-PAT-NO: 4079180

DOCUMENT-IDENTIFIER: US 4079180 A
See image for Certificate of Correction

TITLE: Process for preparing 7-aminocephalosporanic acid derivatives

DATE-ISSUED: March 14, 1978

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Suzuki; Nobuyuki	Hyuga	N/A	N/A	JA
Sowa; Tsuneo	Nobeoka	N/A	N/A	JA
Murakami; Masahiro	Nobeoka	N/A	N/A	JA

APPL-NO: 05/ 650701

DATE FILED: January 20, 1976

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
JA	50-8636	January 22, 1975
JA	50-83574	July 9, 1975
JA	50-83575	July 9, 1975

US-CL-CURRENT: 540/224, 540/230

ABSTRACT:

7-Aminocephalosporanic acid derivatives represented by the general formula (III), ##STR1## wherein X is hydrogen, hydroxyl, acetate or a nucleophilic residue, which are useful as a starting material for the synthesis of cephalosporin type antibiotics low in toxicity and broad in pharmacological effect can be easily prepared by allowing to react cephalosporin C or its derivative represented by the general formula (I), ##STR2## wherein X is as defined above, or a salt thereof with an .alpha.-keto derivative represented by the general formula (II), ##STR3## wherein R.sub.1 is carboxyl, aroyl or amide when R.sub.2 is hydrogen, and is carboxyl when R.sub.2 is alkyl or aryl, or its salt. In this case, the yield of the 7-aminocephalosporanic acid derivatives can be remarkably improved by carrying out the reaction in the presence of hydrogen peroxide. The yield can be further improved by adding thiosulfuric acid or a salt thereof after the completion of the reaction to decompose the unreacted hydrogen peroxide.

20 Claims, 0 Drawing figures

Exemplary Claim Number: 1

---------- KWIC --------

Brief Summary Text - BSTX (5):

However, the above-mentioned processes have such disadvantages that enormous equipments are required for the commercial scale production of **D-amino acid oxidase, that sodium axide or the like enzyme inhibitor,** which is injurious to the human body, is required to be used in large quantities, and that the stable

production of the end product is effected with difficulty, and hence are not always said to be advantageous as commercial scale processes.

US-PAT-NO: 3801458

DOCUMENT-IDENTIFIER: US 3801458 A

TITLE: PROCESS FOR PREPARING CEPHALOSPORIN DERIVATIVES

DATE-ISSUED: April 2, 1974

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Fildes; Robert Anthony	Bouth near Ulverston	N/A	N/A	EN
Potts; James Rowland	Marlow	N/A	N/A	EN
Farthing; John Eaton	Southall	N/A	N/A	EN

APPL-NO: 05/ 245258

DATE FILED: April 18, 1972

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
GB	10566/71	April 21, 1971
GB	10566/71	March 28, 1971

US-CL-CURRENT: 435/47, 435/174 , 435/184 , 435/191 , 435/25 , 435/911

ABSTRACT:

A process for the preparation of a 7.beta.-acylamido-cephalosporin having a 7.beta.-substituent selected from 5-carboxy-5-oxopentanamido and 4-carboxybutanamido includes the step of contacting a corresponding compound having a 7.beta.-(D-5-amino-5-carboxypentanamido) group with activated cells of Trigonopsis variabilis under aerobic conditions, catalase activity being present in said cells when the desired product has a 7.beta.-(5-carboxy-5-oxopentanamido) group.

13 Claims, 0 Drawing figures

---------- KWIC ---------

Brief Summary Text - BSTX (16):

Secondly, it has been found that the D-amino acid oxidase enzyme in activated cells of Trigonopsis variabilis is less easily inhibited or inactivated than the isolated enzyme when used in broths resulting from the fermentation of Cephalosporium acremonium Brotzu. This is a point of much practical importance, since for convenience it is often desired to oxidise cephalosporin C without isolating it from the fermentation broth. Sucn isolation is notoriously difficult, by reason of the amphoteric nature of the compound, and further processing of the cephalosporin C without isolation is practically very advantageous. It was found that the fermentation broth, even after partial purification such as by removal of mycelium and precipitation of protein, contained factors which tended to inhibit fungal D-amino acid oxidases. For this reason, a large excess of enzyme was necessary to ensure satisfactory reaction.

US-PAT-NO: 3658649

DOCUMENT-IDENTIFIER: US 3658649 A

TITLE: CEPHALOSPORIN DERIVATIVES

DATE-ISSUED: April 25, 1972

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Arnold; Benjamin Harry	Slough	N/A	N/A	EN
Fildes; Robert Anthony	Chesham	N/A	N/A	EN
Gilbert; David Arthur	Slough	N/A	N/A	EN

APPL-NO: 04/ 846963

DATE FILED: August 1, 1969

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
GB	37,113/68	August 2, 1968

US-CL-CURRENT: 435/47, 435/191 , 435/911 , 435/913 , 435/915 , 435/919 , 540/217 , 540/219 , 540/222 , 540/230

ABSTRACT:

A process is disclosed for the preparation of a 7.beta.-(4-carboxybutanamide) ceph-3-3em-4-carboxylic acid or a 7.beta.-(5-carboxy-5-oxopentamido) ceph-3-em-4-carboxylic acid by subjecting a 7.beta.-(D-5-amino-5-carboxypentamido) ceph-2-em-4-carboxylic acid to the action of a cell-free fungal D-amino acid oxidase. The modified cephalosporin compounds produced exhibit antimicrobial activity and are useful as presursors in the synthesis of 7-aminocephalosporanic acid and 7.beta.-acylamido analogues of cephalosporin C.

13 Claims, 0 Drawing figures

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Detailed Description Text - DETX (13):

Compounds of formula (I) wherein R is the group --COOH are prepared by reacting the appropriate compound of formula (II) with **D-amino acid oxidase either in the absence of catalase or by inhibiting any catalase present in the D-amino acid oxidase**. It is not normally necessary to purify the **D-amino acid oxidase to remove all traces of catalase since the activity of the latter can be inhibited** where necessary. Suitable catalase inhibitors are ascorbic acid, 3-amino-1,2,3-triazole and inorganic azides. Sodium azide is particularly preferred. The level of sodium azide may be as low as 1 mM when using D-amino acid oxidase extracts but when using acetone powders up to 100 mM or even more may be desirable.

Claims Text - CLTX (10):

10. The process of claim 1 wherein catalase is absent or any catalase present in the **D-amino acid oxidase is inhibited** when a 7.beta.-(4-carboxybutanamido) ceph-3-em-4-carboxylic acid or a salt thereof is

prepared.

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	4067	d adj (amino acid or aspartate) adj oxidase$ or dao or ddo or daao	US-PGPUB; USPAT	ADJ	OFF	2005/01/11 16:02
L2	36	1 near8 inhibit$	US-PGPUB; USPAT	ADJ	OFF	2005/01/11 16:02
L3	5	1 same (schizophrenia or dression or bipolar)	US-PGPUB; USPAT	ADJ	OFF	2005/01/11 16:03

PGPUB-DOCUMENT-NUMBER: 20040157926

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040157926 A1

TITLE: Pharmaceutical compositions for the treatment of movement disorders

PUBLICATION-DATE: August 12, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Heresco-Levy, Uriel	Jerusalem	NY	IL	
Javitt, Daniel C.	Bardonia		US	

APPL-NO: 10/ 744452

DATE FILED: December 23, 2003

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	DOC-ID	APPL-DATE
IL	154,318	2003IL-154,318	February 6, 2003

US-CL-CURRENT: 514/561

ABSTRACT:

The invention provides a pharmaceutical composition, medical food, dietary supplement or micronutrient for the treatment of a movement disorder comprising an NMDAR agonist or partial agonist as active ingredient therein in combination with a pharmaceutically acceptable carrier.

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Detail Description Paragraph - DETX (44):

[0053] Chumakov I, Blumenfeld M, Guerassimenko O, Cavarec L, Palicio M, Abderrahim H, Bougueleret L, et al. Genetic and physiological data implicating the new human gene G72 and the gene for D-amino acid oxidase in schizophrenia. Proc Natl Acad Sci USA 2002;99(21):13675-80.

PGPUB-DOCUMENT-NUMBER: 20030185754

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030185754 A1

TITLE: Treatment of CNS disorders using D-amino acid oxidase and D-aspartate oxidase antagonists

PUBLICATION-DATE: October 2, 2003

US-CL-CURRENT: 424/9.2, 800/3

APPL-NO: 10/ 051681

DATE FILED: January 16, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60261883 20010116 US

non-provisional-of-provisional 60305445 20010713 US

non-provisional-of-provisional 60333881 20011119 US

RELATED APPLICATIONS

[0001] This application claims priority from U.S. Provisional Patent Application Serial Nos. 60/261,883, filed Jan. 16, 2001; 60/305,445, filed Jul. 13, 2001; 60/___,___, filed Oct. 22, 2001; and 60/333,881 filed Nov. 19, 2001, which disclosures are hereby incorporated by reference in their entireties.

PGPUB-DOCUMENT-NUMBER: 20030166554

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030166554 A1

TITLE: Treatment of CNS disorders using D-amino acid oxidase and D-aspartate oxidase antagonists

PUBLICATION-DATE: September 4, 2003

US-CL-CURRENT: 514/12, 424/9.2 , 514/227.5 , 514/231.5 , 514/253.01 , 514/340 , 514/357 , 514/89 , 800/3

APPL-NO: 10/ 211160

DATE FILED: August 1, 2002

RELATED-US-APPL-DATA:

child 10211160 A1 20020801

parent continuation-in-part-of 10051681 20020116 US PENDING

non-provisional-of-provisional 60261883 20010116 US

non-provisional-of-provisional 60305445 20010713 US

non-provisional-of-provisional 60345211 20011022 US

non-provisional-of-provisional 60333881 20011119 US

RELATED APPLICATIONS

[0001] This application is a continuation-in-part of U.S. Ser. No. 10/051,681 claims priority from U.S. Provisional Patent Application Serial Nos. 60/261,883, filed Jan. 16, 2001; 60/305,445, filed Jul. 13, 2001; 60/345,211, filed Oct. 22, 2001; and 60/333,881 filed Nov. 19, 2001, which disclosures are hereby incorporated by reference in their entireties.

PGPUB-DOCUMENT-NUMBER: 20030162825

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030162825 A1

TITLE: D-amino acid oxidase inhibitors for learning and memory

PUBLICATION-DATE: August 28, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Heefner, Donald L.	Hudson	MA	US	
Currie, Mark G.	Sterling	MA	US	
Rossi, Richard Filip JR.	Norton	MA	US	
Zepp, Charles M.	Hardwick	MA	US	

APPL-NO: 10/ 292368

DATE FILED: November 12, 2002

RELATED-US-APPL-DATA:

non-provisional-of-provisional 60332343 20011109 US

US-CL-CURRENT: 514/419, 514/290 , 514/423 , 514/461

ABSTRACT:

Methods and pharmaceutical compositions which inhibit the activity of D-amino acid oxidase (DAO) are disclosed. Inhibition of DAO improves memory, learning and cognition in individuals suffering from neurodegenerative diseases such as Alzheimer's, Huntington's or Parkinson's diseases; the methods and pharmaceutical compositions which inhibit the activity of DAO also improve cognitive dysfunctions associated with aging and improve catatonic schizophrenia. Several genera of heterocycle-2-carboxylic acids are disclosed as DAO inhibitors.

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority from U.S. provisional application, serial No. 60/332,343, filed Nov. 9, 2001, the entire disclosure of which is incorporated herein by reference.

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Abstract Paragraph - ABTX (1):

Methods and pharmaceutical compositions which inhibit the activity of D-amino acid oxidase (DAO) are disclosed. Inhibition of DAO improves memory, learning and cognition in individuals suffering from neurodegenerative diseases such as Alzheimer's, Huntington's or Parkinson's diseases; the methods and pharmaceutical compositions which inhibit the activity of DAO also improve cognitive dysfunctions associated with aging and improve catatonic schizophrenia. Several genera of heterocycle-2-carboxylic acids are disclosed as DAO inhibitors.

Summary of Invention Paragraph - BSTX (25):

[0023] In a second aspect the invention relates to methods for treating a condition chosen from epilepsy, neurotoxic injury, dementia, schizophrenia and neurodegenerative disease comprising administering a therapeutically effective amount of a D-amino acid oxidase (DAO) inhibitor.

Detail Description Paragraph - DETX (3):

[0031] The present invention relates to methods and pharmaceutical compositions which inhibit the activity of DAO, thereby improving memory, learning and cognition in individuals suffering from neurodegenerative diseases such as Alzheimer's, Huntington's or Parkinson's diseases; the methods and pharmaceutical compositions which inhibit the activity of DAO also improve cognitive dysfunctions associated with aging and improve catatonic schizophrenia. DAO inhibitors can also be used in conjunction with therapy involving administration of D-serine or an analog thereof, such as a salt of D-serine, an ester of D-serine, alkylated D-serine, or a precursor of D-serine, or can be used in conjunction with therapy involving administration of antipsychotics, antidepressants, psychostimulants, and/or Alzheimer's disease therapeutics. Examples of disorders that can be treated by the methods of the invention include schizophrenia, autism, depression, benign forgetfulness, childhood learning disorders, close head injury, and attention deficit disorder.

Detail Description Paragraph - DETX (25):

[0053] The invention offers several advantages over many art-known methods for treating neuropsychiatric disorders. For example, unlike many conventional antipsychotic therapeutics, DAO inhibitors can produce a desirable reduction in the cognitive symptoms of schizophrenia. Conventional antipsychotics often lead to tardive dyskinesia (irreversible involuntary movement disorder), extra pyramidal symptoms, and akathesia.

Detail Description Paragraph - DETX (42):

[0070] In a second aspect the invention relates to methods for treating a condition chosen from epilepsy, neurotoxic injury, dementia, schizophrenia and neurodegenerative disease comprising administering a therapeutically effective amount of a D-amino acid oxidase (DAO) inhibitor. Neurodegenerative diseases may include Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, Down syndrome, neuropathic pain, dementia, stroke, mental retardation, ADHD and schizophrenia. Both the first aspect of the invention (learning and memory) and this second aspect envision the use of any and all D-amino acid oxidase (DAO) inhibitors in the method of treatment. However, due to the peculiarities of patent law, and having nothing whatever to do with the scope of the inventors' conception of the invention, certain DAO inhibitors appear from a preliminary search of the literature ineligible to be claimed for the second utility. Thus, for example, indole-2-carboxylic acid, 5-chloroindole-2-carboxylic acid, 5-methoxyindole-2-carboxylic acid and compounds of the generic formula 8

Detail Description Paragraph - DETX (43):

[0071] while they are part of the inventive concept, have been excluded from the claims to treating epilepsy, neurotoxic injury, dementia, schizophrenia and neurodegenerative disease. Excluded genera are those wherein m is 1 to 4; R.sup.3a is hydrogen or methyl; R.sup.5a, R.sup.6a, R.sup.7a and R.sup.8a are chosen from hydrogen and halogen; and R.sup.11 is chosen from hydroxy, lower alkoxy, di(lower alkyl)amino and sulfonamide. It may be found upon examination that methods employing certain members of the excluded genera are patentable to the inventors in this application or that additional species and genera not presently excluded are not patentable to the inventors in this application. In either case, the exclusion of species and genera in applicants' claims are to be considered artifacts of patent prosecution and not reflective of the

inventors' concept or description of their invention, which encompasses all DAO inhibitors.

Detail Description Paragraph - DETX (44):
[0072] In a particular embodiment, DAO inhibitors for treating epilepsy, neurotoxic injury, dementia, schizophrenia, if neurodegenerative disease are compounds of formula 9

Detail Description Paragraph - DETX (51):
[0079] If desired, a pharmaceutical composition containing one or more of the subject DAO inhibitors can be administered to a patient suffering from schizophrenia along with, or in sequence with, a drug for treating schizophrenia (e.g., olanzapine, clozapine, haloperidol, and the like). Similarly, the subject DAO inhibitors can be used in combination with, or in sequence with, other antipsychotics (e.g., "typical," "atypical," and depot antipsychotics for treating schizophrenia and other psychotic conditions), psychostimulants (for treating attention deficit disorder, depression, or learning disorders), or Alzheimer's disease therapeutics (for treating Alzheimer's disease). Such pharmaceutical compositions and methods for conjoint therapies are included within the invention.

Claims Text - CLTX (7):
7. A method for treating a condition chosen from epilepsy, neurotoxic injury, dementia, schizophrenia and neurodegenerative disease comprising administering to a patient in need of treatment a therapeutically effective amount of a D-amino acid oxidase (DAO) inhibitor, with the proviso that said DAO inhibitor is not indole-2-carboxylic acid, 5-chloroindole-2-carboxylic acid, 5-methoxyindole-2-carboxylic acid or a compound of the generic formula 26wherein m is 1 to 4 R.sup.3a is hydrogen or methyl; R.sup.5a, R.sup.6a, R.sup.7a and R.sup.8a are chosen from hydrogen and halogen; and R.sup.11 is chosen from hydroxy, lower alkoxy, di(lower alkyl)amino and sulfonamide.

Claims Text - CLTX (14):
14. A method for treating a condition chosen from Parkinson's disease, Alzheimer's disease, Huntington's disease, epilepsy, neuropathic pain, dementia, ADHD and schizophrenia comprising administering to a patient in need of treatment a therapeutically effective amount of a D-amino acid oxidase inhibitor having an IC.sub.50 less than 10 .mu.M against porcine kidney D-amino acid oxidase.

US-PAT-NO: 4704544

DOCUMENT-IDENTIFIER: US 4704544 A

TITLE: Complementary current mirror logic

DATE-ISSUED: November 3, 1987

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Horwitz; Christopher M.	Sydney	N/A	N/A	AU

APPL-NO: 06/ 854543

DATE FILED: April 22, 1986

US-CL-CURRENT: 326/35, 326/124 , 326/127 , 326/129

ABSTRACT:

A new logic circuit construction in which gates are formed by appropriate interconnections of complementary current-mirror cells. With a signal applied, the resulting logic circuit draws a current drain which rises with power supply voltage, as does the speed of the circuit. With no signal the current drain of the circuit is small. Clocked circuits using this logic can use one clock line. With three states available in the clock line, a non-overlapping two-phase clock is automatically obtained with a simple oscillating signal. This logic circuit is also capable of providing a weighted input or output, enabling threshold logic ("multiple-valued logic") to be performed.

26 Claims, 24 Drawing figures

Exemplary Claim Number: 1

Number of Drawing Sheets: 7

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Detailed Description Text - DETX (2):

The elements making up an embodiment of the present invention are shown in FIG. 1. In FIG. 1(a), Q.sub.2 performs as a pull-up transistor, controlled by the diode-connected transistor Q.sub.1. An input current I.sub.in into Q.sub.1 is reflected into an output current I.sub.out in the output transistor Q.sub.2 having the same magnitude and polarity. This is the well-known "current mirror" action used extensively in analogue integrated circuits and even in multiple-valued digital integrated circuits based on the I.sup.2 L logic family (see K. Hart, A. Slob, "Integrated injection logic--A new approach to LSI," IEEE Journal of Solid State Circuits, vol. SC-7, October 1972, pages 346-351; and T. T. Dao, "Threshold I.sup.2 L and its application in binary symmetric functions and multi-valued logic", IEEE Journal of Solid State Circuits, Vol SC-12, October 1977, pages 463-475). There are however two differences between the above I.sup.2 L circuits and the logic of the present invention; firstly I.sup.2 L requires that every gate input have an "Integrated Injection" of current, and secondly the logic of the present invention utilises two polarities of basic cell, the first cell which is illustrated in FIG. 1(a) employing Q.sub.1 and Q.sub.2 to perform an inverting pull-up function, and the

second cell which is illustrated in FIG. 1(c) employing Q.sub.3 and Q.sub.4 to perform an inverting pull-down function. No commonly used **bipolar** logic uses this complementary cell design. CMOS is in some respects similar, with its use of complementary N-and P-channel field effect transistors. The schematic symbols for the basic elements of FIG. 1(a) & (c) are illustrated in FIGS. 1(b) & (d) respectively.